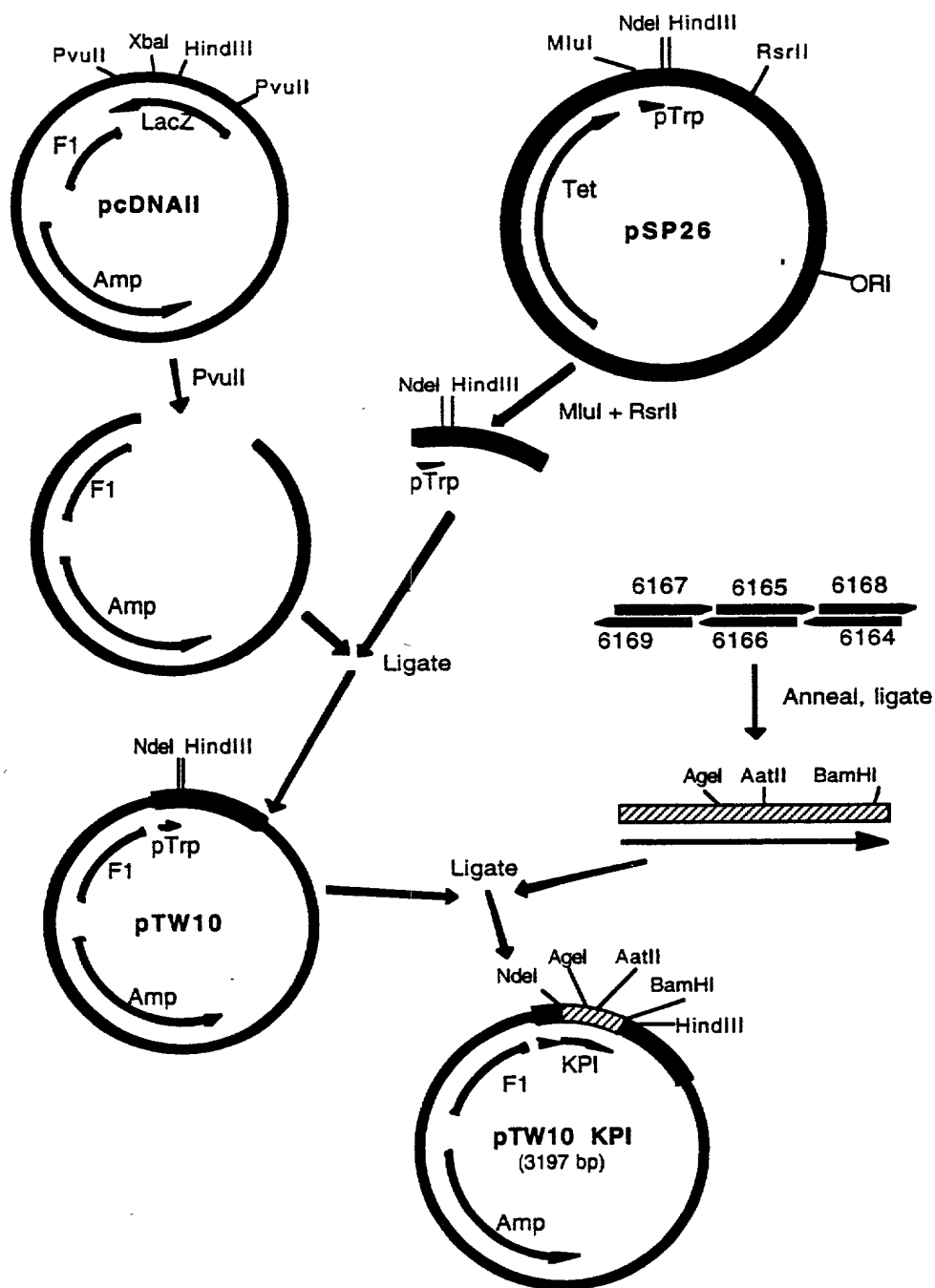


Figure 1



Title: PROTEASE INHIBITOR  
PEPTIDES

Inventor(s): R. Tyler WHITE et al.  
Appl. No.: 09/201,715

Figure 2

NdeI  
TATG AAA CAA AGC ACT ATT GCA CTG GCA CTC TTA CCG TTA CTG TTT ACC CCT GTG ACA AAA  
AC TTT GTT TCG TGA TAA CGT GAC CGT GAG AAT GGC AAT GAC AAA TGG GGA CAC TGT TTT  
►Met Lys Gln Ser Thr Ile Ala Leu Ala Leu Leu Pro Leu Leu Phe Thr Pro Val Thr Lys

KPI  
GCG GAG GTG TGC TCT GAA CAA GCT GAG ACC GGT CCG TGC CGT GCA ATG ATC TCC CGC TGG  
CGG CTC CAC ACG AGA CTT GTT CGA CTC TGG CCA GGC ACG GCA CGT TAC TAG AGG GCG ACC  
►Ala Glu Val Cys Ser Glu Gln Ala Glu Thr Gly Pro Cys Arg Ala Met Ile Ser Arg Trp

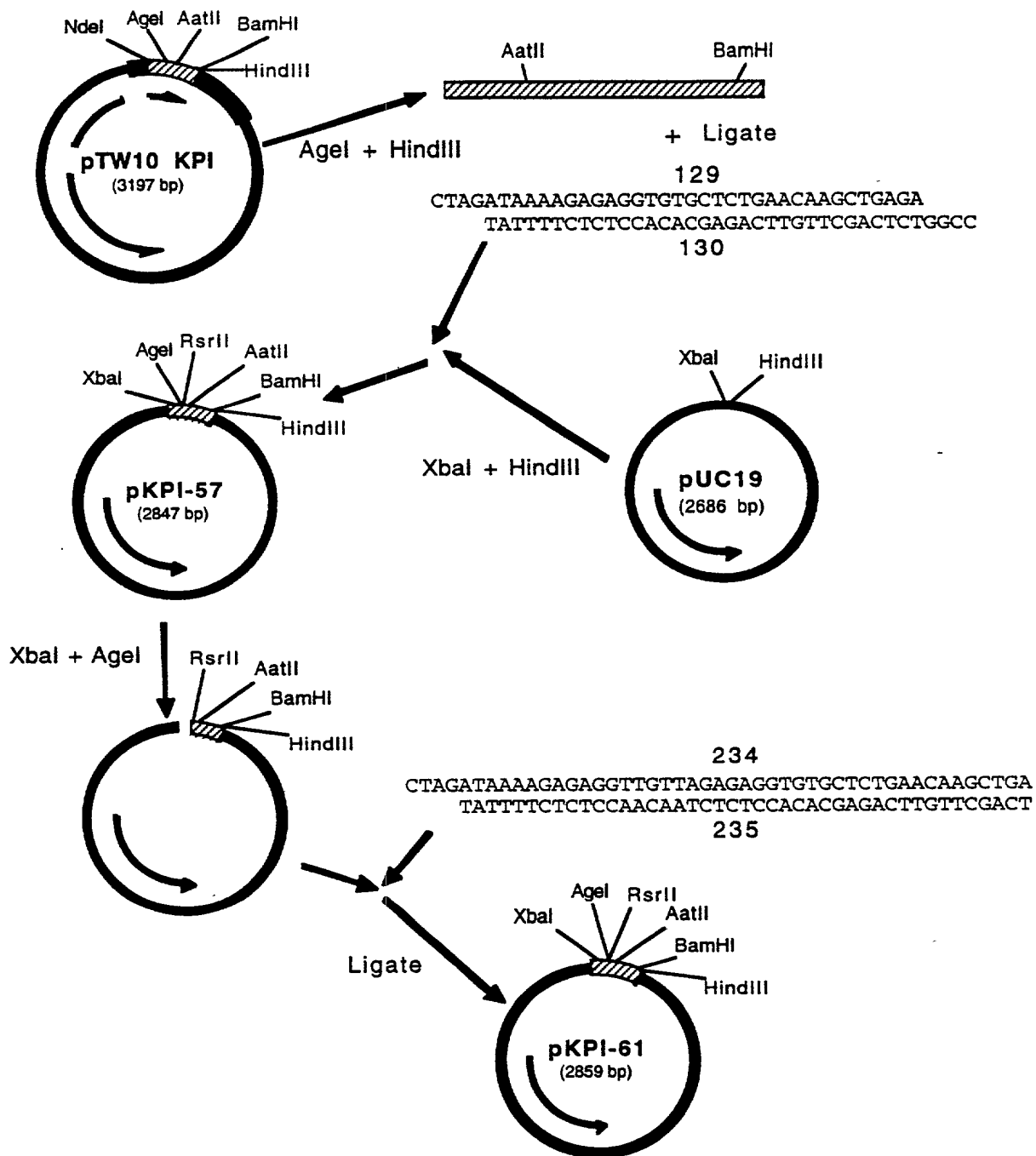
AgeI  
TAC TTT GAC GTC ACT GAA GGT AAG TGC GCT CCA TTC TTT TAC GGC GGT TGC GGC GGC AAC  
ATG AAA CTG CAG TGA CTT CCA TTC ACG CGA GGT AAG AAA ATG CCG CCA ACG CCG CCG TTG  
►Tyr Phe Asp Val Thr Glu Gly Lys Cys Ala Pro Phe Phe Tyr Gly Gly Cys Gly Gly Asn

AatII  
CGT AAC AAC TTT GAC ACT GAA GAG TAC TGC ATG GCA GTG TGC GGA TCC GCT ATT TA  
GCA TTG TTG AAA CTG TGA CTT CTC ATG ACG TAC CGT CAC ACG CCT AGG CGA TAA ATT CGA  
►Arg Asn Asn Phe Asp Thr Glu Glu Tyr Cys Met Ala Val Cys Gly Ser Ala Ile

BamHI  
HindIII

20076604-034902

Figure 3



Appl. No.: 09/201,715

Figure 4

XbaI

KPI (1-57)

RsrII

Agel

AatII

BamHI

HindIII

CTA GAT AAA AGA GAG GTG TGC TCT GAA CAA GCT GAG ACC GGT CCG TGC CGT  
TA TTT TCT CTC CAC ACG AGA CTT GTT CGA CTC TGG CCA GGC ACG GCA  
▶ Leu Asp Lys Arg Glu Val Cys Ser Glu Gln Ala Glu Thr Gly Pro Cys Arg

GCA ATG ATC TCC CGC TGG TAC TTT GAC GTC ACT GAA GGT AAG TGC GCT CCA  
CGT TAC TAG AGG GCG ACC ATG AAA CTG CAG TGA CTT CCA TTC ACG CGA GGT  
▶ Ala Met Ile Ser Arg Trp Tyr Phe Asp Val Thr Glu Gly Lys Cys Ala Pro

TTC TTT TAC GGC GGT TGC GGC GGC AAC CGT AAC AAC TTT GAC ACT GAA GAG  
AAG AAA ATG CCG CCA ACG CCG CCG TTG GCA TTG TTG AAA CTG TGA CTT CTC  
▶ Phe Phe Tyr Gly Gly Cys Gly Gly Asn Arg Asn Asn Phe Asp Thr Glu Glu

TAC TGC ATG GCA GTG TGC GGA TCC GCT ATT TA  
ATG ACG TAC CGT CAC ACG OCT AGG CGA TAA ATT CGA  
▶ Tyr Cys Met Ala Val Cys Gly Ser Ala Ile

[illegible]

Title: PROTEASE INHIBITOR  
PEPTIDES  
Inventor(s): R. Tyler WHITE et al.  
Appl. No.: 09/201,715

Figure 5

RsrII

XbaI                      KPI (-4-57)                      AgeI

CTA GAT AAA AGA GAG GTT GTT AGA GAG GTG TGC TCT GAA CAA GCT GAG ACC GGT  
TA TTT TCT CTC CAA CAA TCT CTC CAC ACG AGA CTT GTT CGA CTC TGG CCA  
▶ Leu Asp Lys Arg Glu Val Val Arg Glu Val Cys Ser Glu Gln Ala Glu Thr Gly

AatII

CCG TGC CGT GCA ATG ATC TCC CGC TGG TAC TTT GAC GTC ACT GAA GGT AAG TGC  
GGC ACG GCA CGT TAC TAG AGG GCG ACC ATG AAA CTG CAG TGA CTT CCA TTC ACG  
▶ Pro Cys Arg Ala Met Ile Ser Arg Trp Tyr Phe Asp Val Thr Glu Gly Lys Cys

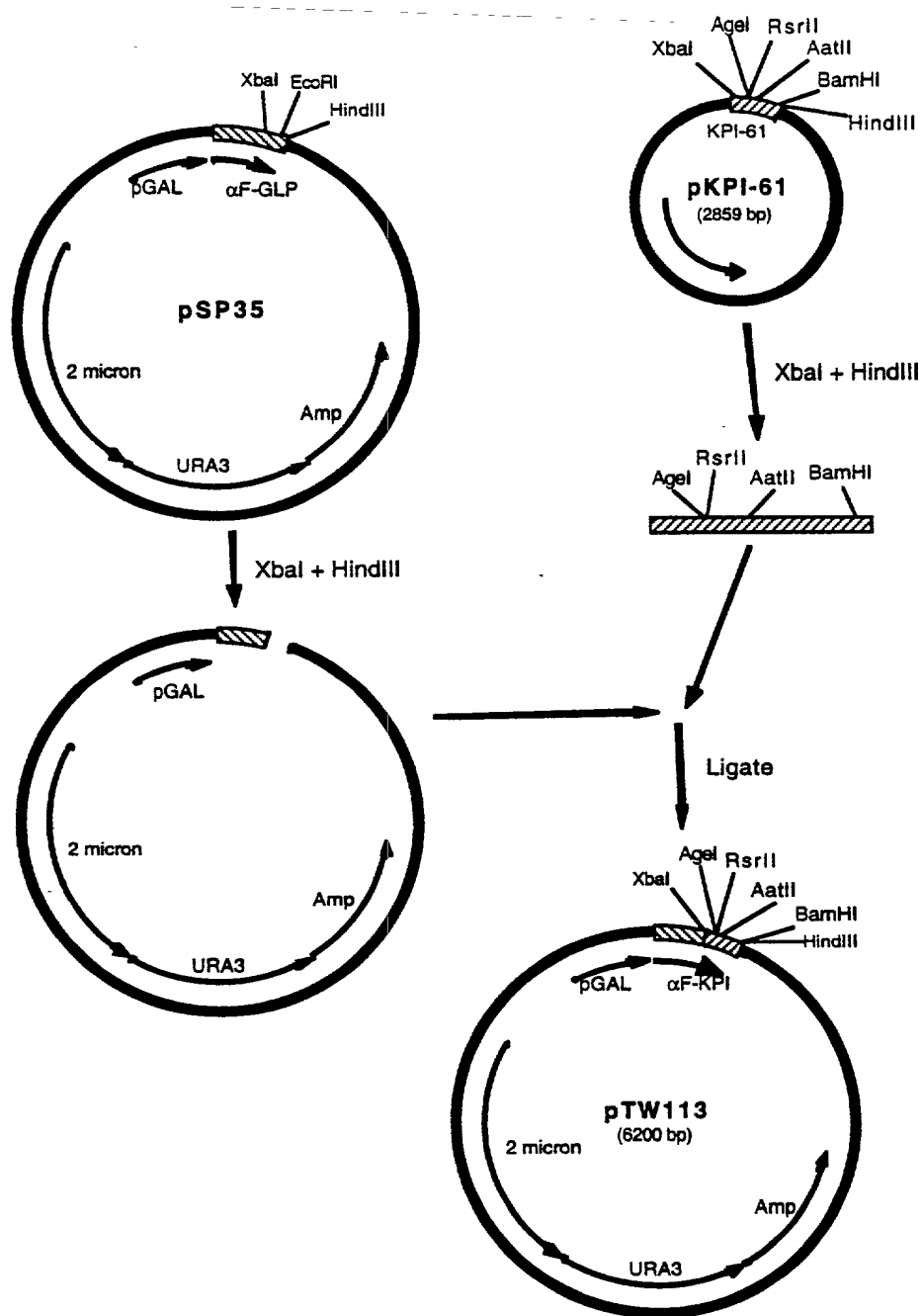
GCT CCA TTC TTT TAC GGC GGT TGC GGC GGC AAC CGT AAC AAC TTT GAC ACT GAA  
CGA GGT AAG AAA ATG CCG CCA ACG CCG CCG TTG GCA TTG TTG AAA CTG TGA CTT  
▶ Ala Pro Phe Phe Tyr Gly Gly Cys Gly Gly Asn Arg Asn Asn Phe Asp Thr Glu

BamHI                      HindIII

GAG TAC TGC ATG GCA GTG TGC GGA TCC GCT ATT TA  
CTC ATG ACG TAC CGT CAC ACG CCT AGG CGA TAA ATT CGA  
▶ Glu Tyr Cys Met Ala Val Cys Gly Ser Ala Ile

20061201 140952001

Figure 6

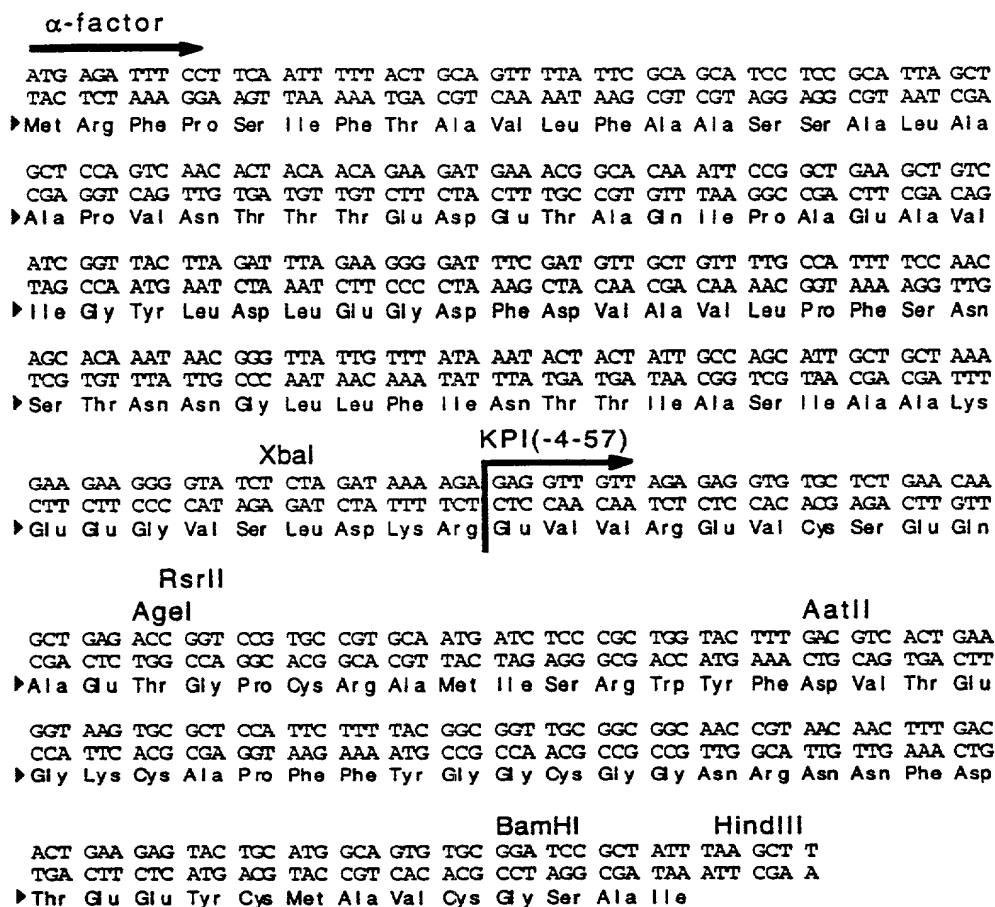


Title: PROTEASE INHIBITOR  
PEPTIDES

Inventor(s): R. Tyler WHITE et al.

Appl. No.: 09/201,715

Figure 7



20075604-023902

Title: PROTEASE INHIBITOR  
PEPTIDES

Inventor(s): R. Tyler WHITE et al.  
Appl. No.: 09/201,715

Figure8

KPI(-4-57)

Glu - Val - Val - Arg - Glu - Val - Cys - Ser - Glu - Gln - Ala  
-4 -3 -2 -1 1 2 3 4 5 6 7

Glu - Thr - Gly - Pro - Cys - Arg - Ala - Met - Ile - Ser - Arg  
8 9 10 11 12 13 14 15 16 17 18

Trp - Tyr - Phe - Asp - Val - Thr - Glu - Gly - Lys - Cys - Ala  
19 20 21 22 23 24 25 26 27 28 29

Pro - Phe - Phe - Tyr - Gly - Gly - Cys - Gly - Gly - Asn - Arg  
30 31 32 33 34 35 36 37 38 39 40

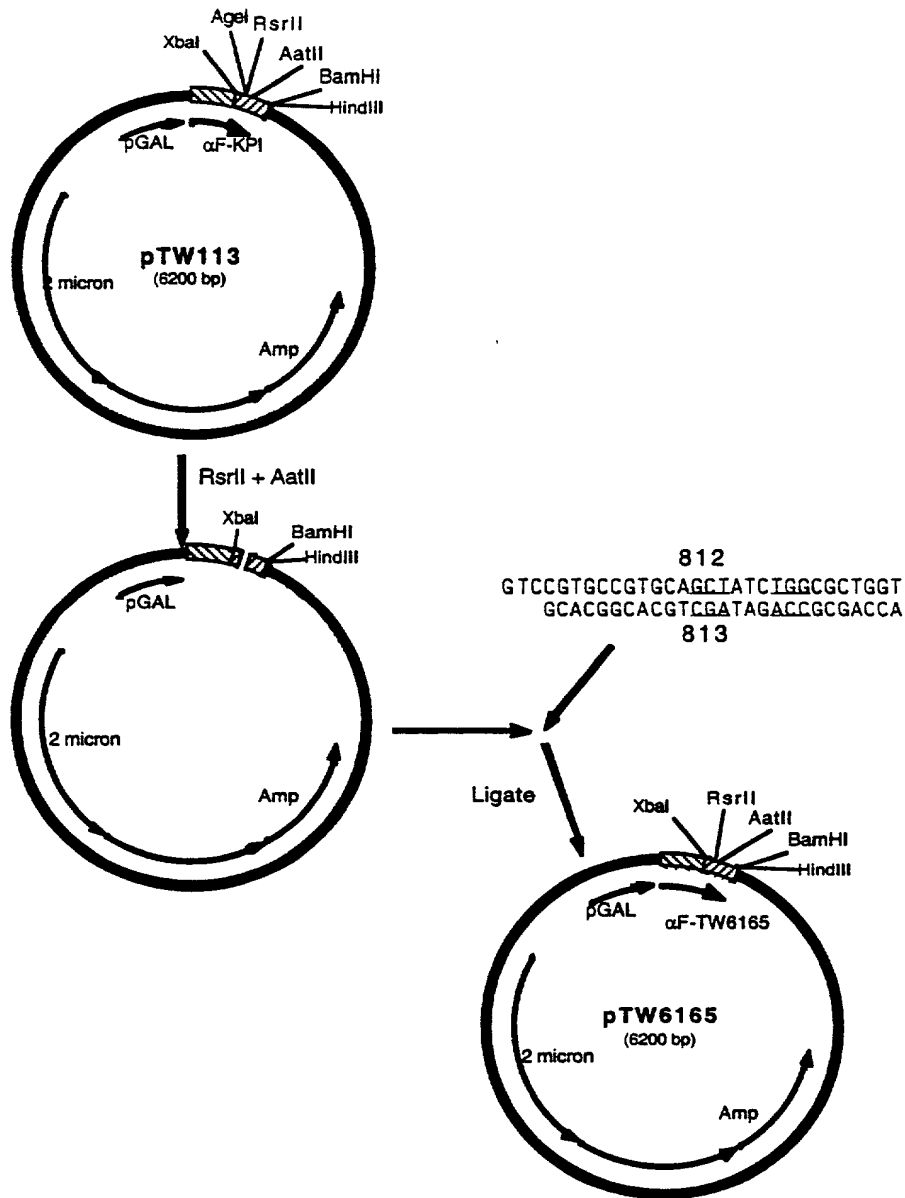
Asn - Asn - Phe - Asp - Thr - Glu - Glu - Tyr - Cys - Met - Ala  
41 42 43 44 45 46 47 48 49 50 51

Val - Cys - Gly - Ser - Ala - Ile  
52 53 54 55 56 57

206TED-4099X00F



Figure 9



20070604.021902

# Title: PROTEASE INHIBITOR

## PEPTIDES

Inventor(s): R. Tyler WHITE et al.

Appl. No.: 09/201,715

Figure 10

pTW 6165

α-factor

ATG AGA TTT CCT TCA ATT TTT ACT GCA GTT TTA TTC GCA GCA TCC TCC GCA TTA GCT  
TAC TCT AAA GGA AGT TAA AAA TGA CGT CAA AAT AAG CGT CGT AGG AGG CGT AAT CGA  
▶ Met Arg Phe Pro Ser Ile Phe Thr Ala Val Leu Phe Ala Ala Ser Ser Ala Leu Ala  
  
GCT CCA GTC AAC ACT ACA ACA GAA GAT GAA ACG GCA CAA ATT CCG GCT GAA GCT GTC  
CGA GGT CAG TTG TGA TGT TGT CTT CTA CTT TGC CGT GTT TAA GGC CGA CTT CGA CAG  
▶ Ala Pro Val Asn Thr Thr Thr Glu Asp Glu Thr Ala Gln Ile Pro Ala Glu Ala Val  
  
ATC GGT TAC TTA GAT TTA GAA GGG GAT TTC GAT GTT GCT GTT TTG CCA TTT TCC AAC  
TAG CCA ATG AAT CTA AAT CTT CCC CTA AAG CTA CAA CGA CAA AAC GGT AAA AGG TTG  
▶ Ile Gly Tyr Leu Asp Leu Glu Gly Asp Phe Asp Val Ala Val Leu Pro Phe Ser Asn  
  
AGC ACA AAT AAC GGG TTA TTG TTT ATA AAT ACT ACT ATT GCC AGC ATT GCT GCT AAA  
TCG TGT TTA TTG CCC AAT AAC AAA TAT TTA TGA TGA TAA CCG TCG TAA CGA CGA TTT  
▶ Ser Thr Asn Asn Gly Leu Leu Phe Ile Asn Thr Thr Ile Ala Ser Ile Ala Ala Lys

XbaI

KPI(-4-57; M15A; S17W)

GAA GAA GGG GTA TCT CTA GAT AAA AGA GAG GTT GTT AGA GAG GTG TGC TCT GAA CAA  
CTT CTT CCC CAT AGA GAT CTA TTT TCT CTC CAA CAA TCT CTC CAC ACG AGA CTT GTT  
▶ Glu Glu Gly Val Ser Leu Asp Lys Arg Glu Val Val Arg Glu Val Cys Ser Glu Gln

RsrII

AgeI

AatII

GCT GAG ACC GGT CCG TGC CGT GCA GCT ATC TGG CGC TGG TAC TTT GAC GTC ACT GAA  
CGA CTC TGG CCA GGC ACG GCA CGT CGA TAG ACC GCG ACC ATG AAA CTG CAG TGA CTT  
▶ Ala Glu Thr Gly Pro Cys Arg Ala Ala Ile Trp Arg Trp Tyr Phe Asp Val Thr Glu  
  
GGT AAG TGC GCT CCA TTC TTT TAC GGC GGT TGC GGC GGC AAC CGT AAC AAC TTT GAC  
CCA TTC ACG CGA GGT AAG AAA ATG CCG CCA ACG CCG CCG TTG GCA TTG TTG AAA CTG  
▶ Gly Lys Cys Ala Pro Phe Phe Tyr Gly Gly Cys Gly Gly Asn Arg Asn Asn Phe Asp

BamHI

HindIII

ACT GAA GAG TAC TGC ATG GCA GTG TGC GGA TCC GCT ATT TAA GCT T  
TGA CTT CTC ATG ACG TAC CGT CAC ACG CCT AGG CGA TAA ATT CGA A  
▶ Thr Glu Glu Tyr Cys Met Ala Val Cys Gly Ser Ala Ile

2007-09-04 10:09:20

Title: PROTEASE INHIBITOR  
PEPTIDES  
Inventor(s): R. Tyler WHITE et al.  
Appl. No.: 09/201,715

Figure 11

812  
GTCCGTGCCGTGCAGCTATCIGGCGCTGGTACTTTGACGT pTW6165 KPI(-4-57; M15A, S17F)  
GCACGGCACGTGATAGACCGCGACCATGAAAC

813

814  
GTCCGTGCCGTGCAGCTATCIACCGCTGGTACTTTGACGT pTW6166 KPI(-4-57; M15A, S17Y)  
GCACGGCACGTGATAGATGGCGACCATGAAAC

815

867  
GTCCGTGCCGTGCAITIGATCIICCGCTGGTACTTTGACGT pTW6175 KPI(-4-57; M15L, S17F)  
GCACGGCACGTAACTAGAAAGGCGACCATGAAAC

868

1493  
GTCCGTGCCGTGCAITIGATCIACCGCTGGTACTTTGACGT pBG028 KPI(-4-57; M15L, S17Y)  
GCACGGCACGTAACTAGATGGCGACCATGAAAC

1494

925  
GTCCGTGCCGTGCAATGCACITICCGCTGGTACTTTGACGT pTW6183 KPI(-4-57; I16H, S17F)  
GCACGGCACGTACGTGAAGGCGACCATGAAAC

926

927  
GTCCGTGCCGTGCAATGCACIACCGCTGGTACTTTGACGT pTW6184 KPI(-4-57; I16H, S17Y)  
GCACGGCACGTACGTGATGGCGACCATGAAAC

928

929  
GTCCGTGCCGTGCAATGCACITGGCGCTGGTACTTTGACGT pTW6185 KPI(-4-57; I16H, S17W)  
GCACGGCACGTACGTGACCGCGACCATGAAAC

930

863  
GTCCGTGCCGTGCAGCTCACTCCCGCTGGTACTTTGACGT pTW6173 KPI(-4-57; M15A, I16H)  
GCACGGCACGTGAGTGAGGGCGACCATGAAAC

864

865  
GTCCGTGCCGTGCAITIGCACTCCCGCTGGTACTTTGACGT pTW6174 KPI(-4-57; M15L, I16H)  
GCACGGCACGTAACTGAGGGCGACCATGAAAC

866

20076604-021902

Title: PROTEASE INHIBITOR  
PEPTIDES

Inventor(s): R. Tyler WHITE et al.

Appl. No.: 09/201,715

Figure 12

pTW 6166

$\alpha$ -factor

ATG AGA TTT CCT TCA ATT TTT ACT GCA GTT TTA TTC GCA GCA TCC TCC GCA TTA GCT  
TAC TCT AAA GGA AGT TAA AAA TGA CGT CAA AAT AAG CGT CGT AGG AGG CGT AAT CGA  
Met Arg Phe Pro Ser Ile Phe Thr Ala Val Leu Phe Ala Ala Ser Ser Ala Leu Ala  
GCT CCA GTC AAC ACT ACA ACA GAA GAT GAA ACG GCA CAA ATT CCG GCT GAA GCT GTC  
CGA GGT CAG TTG TGA TGT TGT CTT CTA CTT TGC CGT GTT TAA GGC CGA CTT CGA CAG  
Ala Pro Val Asn Thr Thr Thr Glu Asp Glu Thr Ala Gln Ile Pro Ala Glu Ala Val  
ATC GGT TAC TTA GAT TTA GAA GGG GAT TTC GAT GTT GCT GTT TTG CCA TTT TCC AAC  
TAG CCA ATG AAT CTA AAT CTT CCC CTA AAG CTA CAA CGA CAA AAC GGT AAA AGG TTG  
Ile Gly Tyr Leu Asp Leu Glu Gly Asp Phe Asp Val Ala Val Leu Pro Phe Ser Asn  
AGC ACA AAT AAC GGG TTA TTG TTT ATA AAT ACT ACT ATT GCC AGC ATT GCT GCT AAA  
TCG TGT TTA TTG CCC AAT AAC AAA TAT TTA TGA TGA TAA CGG TCG TAA CGA CGA TTT  
Ser Thr Asn Asn Gly Leu Leu Phe Ile Asn Thr Thr Ile Ala Ser Ile Ala Ala Lys

XbaI

KPI(-4-57; M15A, S17Y)

GAA GAA GGG GTA TCT CTA GAT AAA AGA GAG GTT GTT AGA GAG GTG TGC TCT GAA CAA  
CTT CTT CCC CAT AGA GAT CTA TTT TCT CTC CAA CAA TCT CTC CAC ACG AGA CTT GTT  
Glu Glu Gly Val Ser Leu Asp Lys Arg Glu Val Val Arg Glu Val Cys Ser Glu Gln

RsrII

AgeI

AatII

GCT GAG ACC GGT CCG TGC CGT GCA GCT ATC TAC CGC TGG TAC TTT GAC GTC ACT GAA  
CGA CTC TGG CCA GGC ACG GCA CGT CGA TAG ATG GCG ACC ATG AAA CTG CAG TGA CTT  
Ala Glu Thr Gly Pro Cys Arg Ala Ala Ile Tyr Arg Trp Tyr Phe Asp Val Thr Glu  
GGT AAG TGC GCT CCA TTC TTT TAC GGC GGT TGC GGC GGC AAC CGT AAC AAC TTT GAC  
CCA TTC ACG CGA GGT AAG AAA ATG CCG CCA ACG CCG CCG TTG GCA TTG TTG AAA CTG  
Gly Lys Cys Ala Pro Phe Phe Tyr Gly Gly Cys Gly Gly Asn Arg Asn Asn Phe Asp

BamHI

HindIII

ACT GAA GAG TAC TGC ATG GCA GTG TGC GGA TCC GCT ATT TAA GCT T  
TGA CTT CTC ATG ACG TAC CGT CAC ACG CCT AGG CGA TAA ATT CGA A  
Thr Glu Glu Tyr Cys Met Ala Val Cys Gly Ser Ala Ile

10076604-021902

Title: PROTEASE INHIBITOR  
PEPTIDES  
Inventor(s): R. Tyler WHITE et al.  
Appl. No.: 09/201,715

Figure 13

pTW 6175

$\alpha$ -factor

ATG AGA TTT CCT TCA ATT TTT ACT GCA GTT TTA TTC GCA GCA TCC TCC GCA TTA GCT  
TAC TGT AAA GGA AGT TAA AAA TGA CGT CAA AAT AAG CGT CGT AGG AGG CGT AAT CGA  
▶ Met Arg Phe Pro Ser Ile Phe Thr Ala Val Leu Phe Ala Ala Ser Ser Ala Leu Ala  
  
GCT CCA GTC AAC ACT ACA ACA GAA GAT GAA ACG GCA CAA ATT CCG GCT GAA GCT GTC  
CGA GGT CAG TTG TGA TGT TGT CTT CTA CTT TGC CGT GGT TAA GGC CGA CTT CGA CAG  
▶ Ala Pro Val Asn Thr Thr Thr Glu Asp Glu Thr Ala Gln Ile Pro Ala Glu Ala Val  
  
ATC GGT TAC TTA GAT TTA GAA GGG GAT TTC GAT GTT GCT GTT TTG CCA TTT TCC AAC  
TAG CCA ATG AAT CTA AAT CTT CCC CTA AAG CTA CAA CGA CAA AAC GGT AAA AGG TTG  
▶ Ile Gly Tyr Leu Asp Leu Glu Gly Asp Phe Asp Val Ala Val Leu Pro Phe Ser Asn  
  
AGC ACA AAT AAC GGG TTA TTG TTT ATA AAT ACT ACT ATT GCC AGC ATT GCT GCT AAA  
TCG TGT TTA TTG CCC AAT AAC AAA TAT TTA TGA TGA TAA CGG TCG TAA CGA CGA TTT  
▶ Ser Thr Asn Asn Gly Leu Leu Phe Ile Asn Thr Thr Ile Ala Ser Ile Ala Ala Lys

KPI(-4-57; M15L, S17F)

GAA GAA GGG GTA TCT CTA GAT AAA AGA GAG GTT GTT AGA GAG GTG TGC TCT GAA CAA  
CTT CTT CCC CAT AGA GAT CTA TTT TCT CTC CAA CAA TCT CTC CAC ACG AGA CTT GTT  
▶ Glu Glu Gly Val Ser Leu Asp Lys Arg Glu Val Val Arg Glu Val Cys Ser Glu Gln

RsrII

AgeI

AatII

GCT GAG ACC GGT CCG TGC CGT GCA TTG ATC TTC CGC TGG TAC TTT GAC GTC ACT GAA  
CGA CTC TGG CCA GGC ACG GCA CGT AAC TAG AAG GCG ACC ATG AAA CTG CAG TGA CTT  
▶ Ala Glu Thr Gly Pro Cys Arg Ala Leu Ile Phe Arg Trp Tyr Phe Asp Val Thr Glu  
  
GGT AAG TGC GCT CCA TTC TTT TAC GGC GGT TGC GGC GGC AAC CGT AAC AAC TTT GAC  
CCA TTC ACG CGA GGT AAG AAA ATG CCG CCA ACG CCG CCG TTG GCA TTG TTG AAA CTG  
▶ Gly Lys Cys Ala Pro Phe Phe Tyr Gly Gly Cys Gly Gly Asn Arg Asn Asn Phe Asp

BamHI

HindIII

ACT GAA GAG TAC TGC ATG GCA GTG TGC GGA TCC GCT ATT TAA GCT T  
TGA CTT CTC ATG ACG TAC CGT CAC ACG CCT AGG CGA TAA ATT CGA A  
▶ Thr Glu Glu Tyr Cys Met Ala Val Cys Gly Ser Ala Ile

2007604-024902

Title: PROTEASE INHIBITOR  
PEPTIDES  
Inventor(s): R. Tyler WHITE et al.  
Appl. No.: 09/201,715

Figure 14

pBG028

$\alpha$ -factor

ATG AGA TTT CCT TCA ATT TTT ACT GCA GTT TTA TTC GCA GCA TCC TCC GCA TTA GCT  
TAG TCT AAA GGA AGT TAA AAA TGA CGT CAA AAT AAG CGT CGT AGG AGG CGT AAT CGA  
► Met Arg Phe Pro Ser Ile Phe Thr Ala Val Leu Phe Ala Ala Ser Ser Ala Leu Ala  
  
GCT CCA GTC AAC ACT ACA ACA GAA GAT GAA ACG GCA CAA ATT CCG GCT GAA GCT GTC  
CGA GGT CAG TTG TGA TGT CTT CCC CTA CTT TGC CGT GTT TAA GGC CGA CTT CGA CAG  
► Ala Pro Val Asn Thr Thr Thr Glu Asp Glu Thr Ala Gln Ile Pro Ala Glu Ala Val  
  
ATC GGT TAC TTA GAT TTA GAA GGG GAT TTC GAT GTT GCT GTT TTG CCA TTT TCC AAC  
TAG CCA ATG AAT CTA AAT CTT CCC CTA AAG CTA CAA CGA CAA AAC GGT AAA AGG TTG  
► Ile Gly Tyr Leu Asp Leu Glu Gly Asp Phe Asp Val Ala Val Leu Pro Phe Ser Asn  
  
AGC ACA AAT AAC GGG TTA TTG TTT ATA AAT ACT ACT ATT GCC AGC ATT GCT GCT AAA  
TCG TGT TTA TTG CCC AAT AAC AAA TAT TTA TGA TAA CGG TCG TAA CGA CGA TTT  
► Ser Thr Asn Asn Gly Leu Leu Phe Ile Asn Thr Thr Ile Ala Ser Ile Ala Ala Lys

XbaI

KPI(-4-57; M15L, S17Y)

GAA GAA GGG GTA TCT CTA GAT AAA AGA GAG GTT GTT AGA GAG GTG TGC TCT GAA CAA  
CTT CTT CCC CAT AGA GAT CTA TTT TCT CTC CAA CAA TCT CTC CAC ACG AGA CTT GTT  
► Glu Glu Gly Val Ser Leu Asp Lys Arg Glu Val Val Arg Glu Val Cys Ser Glu Gln

RsrII

AgeI

AatII

GCT GAG ACC GGT CCG TGC CGT GCA TTG ATC TAC CGC TGG TAC TTT GAC GTC ACT GAA  
CGA CTC TGG CCA GGC ACG GCA CGT AAC TAG ATG GCG ACC ATG AAA CTG CAG TGA CTT  
► Ala Glu Thr Gly Pro Cys Arg Ala Leu Ile Tyr Arg Trp Tyr Phe Asp Val Thr Glu  
  
GGT AAG TGC GCT CCA TTC TTT TAC GGC GGT TGC GGC GGC AAC CGT AAC AAC TTT GAC  
CCA TTC ACG CGA GGT AAG AAA ATG CCG CCA ACG CCG CCG TTG GCA TTG TTG AAA CTG  
► Gly Lys Cys Ala Pro Phe Phe Tyr Gly Gly Cys Gly Gly Asn Arg Asn Asn Phe Asp

BamHI

HindIII

ACT GAA GAG TAC TGC ATG GCA GTG TGC GGA TCC GCT ATT TAA GCT T  
TGA CTT CTC ATG ACG TAC CGT CAC ACG CCT AGG CGA TAA ATT CGA A  
► Thr Glu Glu Tyr Cys Met Ala Val Cys Gly Ser Ala Ile

10076604-021902

Figure 15

pTW6183

$\alpha$ -factor

ATG AGA TTT CCT TCA ATT TTT ACT GCA GTT TTA TTC GCA GCA TCC TCC GCA TTA GCT  
TAC TCT AAA GGA AGT TAA AAA TGA CGT CAA AAT AAG CGT CGT AGG AGG CGT AAT CGA  
▶ Met Arg Phe Pro Ser Ile Phe Thr Ala Val Leu Phe Ala Ala Ser Ser Ala Leu Ala  
  
GCT CCA GTC AAC ACT ACA ACA GAA GAT GAA ACG GCA CAA ATT CCG GCT GAA GCT GTC  
CGA GGT CAG TTG TGA TGT TGT CTT CTA CTT TGC CGT GTT TAA GGC CGA CTT CGA CAG  
▶ Ala Pro Val Asn Thr Thr Thr Glu Asp Glu Thr Ala Gln Ile Pro Ala Glu Ala Val  
  
ATC GGT TAC TTA GAT TTA GAA GGG GAT TTC GAT GTT GCT GTT TTG CCA TTT TCC AAC  
TAG CCA ATG AAT CTA AAT CTT CCC CTA AAG CTA CAA CGA CAA AAC GGT AAA AGG TTG  
▶ Ile Gly Tyr Leu Asp Leu Glu Gly Asp Phe Asp Val Ala Val Leu Pro Phe Ser Asn  
  
AGC ACA AAT AAC GGG TTA TTG TTT ATA AAT ACT ACT ATT GCC AGC ATT GCT GCT AAA  
TCG TGT TTA TTG CCC AAT AAC AAA TAT TTA TGA TGA TAA CGG TCG TAA CGA CGA TTT  
▶ Ser Thr Asn Asn Gly Leu Leu Phe Ile Asn Thr Thr Ile Ala Ser Ile Ala Ala Lys

KPI(-4-57; I16H, S17F)

XbaI

GAA GAA GGG GTA TCT CTA GAT AAA AGA GAG GTT GTT AGA GAG GTG TGC TCT GAA CAA  
CTT CTT CCC CAT AGA GAT CTA TTT TCT CTC CAA CAA TCT CTC CAC ACG AGA CTT GTT  
▶ Glu Glu Gly Val Ser Leu Asp Lys Arg Glu Val Val Arg Glu Val Cys Ser Glu Gln

RsrII

AgeI

AatII

GCT GAG ACC GGT CCG TGC CGT GCA ATG CAC TTC CGC TGG TAC TTT GAC GTC ACT GAA  
CGA CTC TGG CCA GGC ACG GCA CGT TAC GTG AAG GCG ACC ATG AAA CTG CAG TGA CTT  
▶ Ala Glu Thr Gly Pro Cys Arg Ala Met His Phe Arg Trp Tyr Phe Asp Val Thr Glu  
  
GGT AAG TGC GCT CCA TTC TTT TAC GGC GGT TGC GGC GGC AAC CGT AAC AAC TTT GAC  
CCA TTC ACG CGA GGT AAG AAA ATG CCG CCA ACG CCG CCG TTG GCA TTG TTG AAA CTG  
▶ Gly Lys Cys Ala Pro Phe Phe Tyr Gly Gly Cys Gly Gly Asn Arg Asn Asn Phe Asp

BamHI

HindIII

ACT GAA GAG TAC TGC ATG GCA GTG TGC GGA TCC GCT ATT TAA GCT T  
TGA CTT CTC ATG ACG TAC CGT CAC ACG CCT AGG CGA TAA ATT CGA A  
▶ Thr Glu Glu Tyr Cys Met Ala Val Cys Gly Ser Ala Ile

10076604-021902

Title: PROTEASE INHIBITOR  
PEPTIDES

Inventor(s): R. Tyler WHITE et al.

Appl. No.: 09/201,715

Figure 16

pTW6184

$\alpha$ -factor

ATG AGA TTT CCT TCA ATT TTT ACT GCA GTT TTA TTC GCA GCA TCC TCC GCA TTA GCT  
TAC TCT AAA GGA AGT TAA AAA TGA CGT CAA AAT AAG CGT CGT AGG AGG CGT AAT CGA  
▶ Met Arg Phe Pro Ser Ile Phe Thr Ala Val Leu Phe Ala Ala Ser Ser Ala Leu Ala

GCT CCA GTC AAC ACT ACA ACA GAA GAT GAA ACG GCA CAA ATT CCG GCT GAA GCT GTC  
CGA GGT CAG TTG TGA TGT TGT CTT CTA CTT TGC CGT GTT TAA GGC CGA CTT CGA CAG  
▶ Ala Pro Val Asn Thr Thr Thr Glu Asp Glu Thr Ala Gln Ile Pro Ala Glu Ala Val

ATC GGT TAC TTA GAT TTA GAA GGG GAT TTC GAT GTT GCT GTT TTG CCA TTT TCC AAC  
TAG CCA ATG AAT CTA AAT CTT CCC CTA AAG CTA CAA CGA CAA AAC GGT AAA AGG TTG  
▶ Ile Gly Tyr Leu Asp Leu Glu Gly Asp Phe Asp Val Ala Val Leu Pro Phe Ser Asn

AGC ACA AAT AAC GGG TTA TTG TTT ATA AAT ACT ACT ATT GCC AGC ATT GCT GCT AAA  
TCG TGT TTA TTG CCC AAT AAC AAA TAT TTA TGA TGA TAA CCG TCG TAA CGA CGA TTT  
▶ Ser Thr Asn Asn Gly Leu Leu Phe Ile Asn Thr Thr Ile Ala Ser Ile Ala Ala Lys

XbaI

KPI(-4-57; I16H, S17Y)

GAA GAA GGG GTA TCT CTA GAT AAA AGA GAG GTT GTT AGA GAG GTG TGC TCT GAA CAA  
CTT CTT CCC CAT AGA GAT CTA TTT TCT CTC CAA CAA TCT CTC CAC ACG AGA CTT GTT  
▶ Glu Glu Gly Val Ser Leu Asp Lys Arg Glu Val Val Arg Glu Val Cys Ser Glu Gln

RsrII

AgeI

AatII

GCT GAG ACC GGT CCG TGC CGT GCA ATG CAC TAC CGC TGG TAC TTT GAC GTC ACT GAA  
CGA CTC TGG CCA GGC ACG GCA CGT TAC GTG ATG GCG ACC ATG AAA CTG CAG TGA CTT  
▶ Ala Glu Thr Gly Pro Cys Arg Ala Met His Tyr Arg Trp Tyr Phe Asp Val Thr Glu

GGT AAG TGC GCT CCA TTC TTT TAC GGC GGT TGC GGC GGC AAC CGT AAC AAC TTT GAC  
CCA TTC ACG CGA GGT AAG AAA ATG CCG CCA ACG CCG CCG TTG GCA TTG TTG AAA CTG  
▶ Gly Lys Cys Ala Pro Phe Phe Tyr Gly Gly Cys Gly Gly Asn Arg Asn Asn Phe Asp

BamHI

HindIII

ACT GAA GAG TAC TGC ATG GCA GTG TGC GGA TCC GCT ATT TAA GCT T  
TGA CTT CTC ATG ACG TAC CGT CAC ACG CCT AGG CGA TAA ATT CGA A  
▶ Thr Glu Glu Tyr Cys Met Ala Val Cys Gly Ser Ala Ile

20076604-021902



Figure 17

pTW6185

$\alpha$ -factor

ATG AGA TTT CCT TCA ATT TTT ACT GCA GTT TTA TTC GCA GCA TCC TCC GCA TTA GCT  
TAC TCT AAA GGA AGT TAA AAA TGA CGT CAA AAT AAG CGT CGT AGG AGG CGT AAT CGA  
►Met Arg Phe Pro Ser Ile Phe Thr Ala Val Leu Phe Ala Ala Ser Ser Ala Leu Ala  
  
GCT CCA GTC AAC ACT ACA ACA GAA GAT GAA ACG GCA CAA ATT CCG GCT GAA GCT GTC  
CGA GGT CAG TTG TGA TGT TGT CTT CTA CTT TGC CGT GTT TAA GGC CGA CTT CGA CAG  
►Ala Pro Val Asn Thr Thr Thr Glu Asp Glu Thr Ala Gln Ile Pro Ala Glu Ala Val  
  
ATC GGT TAC TTA GAT TTA GAA GGG GAT TTC GAT GTT GCT GTT TTG CCA TTT TCC AAC  
TAG CCA ATG AAT CTA AAT CTT CCC CTA AAG CTA CAA CGA CAA AAC GGT AAA AGG TTG  
►Ile Gly Tyr Leu Asp Leu Glu Gly Asp Phe Asp Val Ala Val Leu Pro Phe Ser Asn  
  
AGC ACA AAT AAC GGG TTA TTG TTT ATA AAT ACT ACT ATT GCC AGC ATT GCT GCT AAA  
TCG TGT TTA TTG CCC AAT AAC AAA TAT TTA TGA TGA TAA CGG TCG TAA CGA CGA TTT  
►Ser Thr Asn Asn Gly Leu Leu Phe Ile Asn Thr Thr Ile Ala Ser Ile Ala Ala Lys

XbaI

KPI(-4-57; I16H, S17W)

GAA GAA GGG GTA TCT CTA GAT AAA AGA GAG GTT GTT AGA GAG GTG TGC TCT GAA CAA  
CTT CTT CCC CAT AGA GAT CTA TTT TCT CTC CAA CAA TCT CTC CAC ACG AGA CTT GTT  
►Glu Glu Gly Val Ser Leu Asp Lys Arg Glu Val Val Arg Glu Val Cys Ser Glu Gln

RsrII

AgeI

AatII

GCT GAG ACC GGT CCG TGC CGT GCA ATG CAC TGG CGC TGG TAC TTT GAC GTC ACT GAA  
CGA CTC TGG CCA GGC ACG GCA CGT TAC GTG ACC GCG ACC ATG AAA CTG CAG TGA CTT  
►Ala Glu Thr Gly Pro Cys Arg Ala Met His Trp Arg Trp Tyr Phe Asp Val Thr Glu  
  
GGT AAG TGC GCT CCA TTC TTT TAC GGC GGT TGC GGC GGC AAC CGT AAC AAC TTT GAC  
CCA TTC ACG CGA GGT AAG AAA ATG CCG CCA ACG CCG CCG TTG GCA TTG TTG AAA CTG  
►Gly Lys Cys Ala Pro Phe Phe Tyr Gly Gly Cys Gly Gly Asn Arg Asn Asn Phe Asp

BamHI

HindIII

ACT GAA GAG TAC TGC ATG GCA GTG TGC GGA TCC GCT ATT TAA GCT T  
TGA CTT CTC ATG ACG TAC CGT CAC ACG CCT AGG CGA TAA ATT CGA A  
►Thr Glu Glu Tyr Cys Met Ala Val Cys Gly Ser Ala Ile

20070604 10:03:02

Title: PROTEASE INHIBITOR  
PEPTIDES

Inventor(s): R. Tyler WHITE et al.

Appl. No.: 09/201,715

Figure 18

pTW6173

α-factor

ATG AGA TTT CCT TCA ATT TTT ACT GCA GTT TTA TTC GCA GCA TCC TCC GCA TTA GCT  
TAC TCT AAA GGA AGT TAA AAA TGA CGT CAA AAT AAG CGT CGT AGG AGG CGT AAT CGA  
▶ Met Arg Phe Pro Ser Ile Phe Thr Ala Val Leu Phe Ala Ala Ser Ser Ala Leu Ala

GCT CCA GTC AAC ACT ACA ACA GAA GAT GAA ACG GCA CAA ATT CCG GCT GAA GCT GTC  
CGA GGT CAG TTG TGA TGT TGT CTT CTA CTT TGC CGT GTT TAA GGC CGA CTT CGA CAG  
▶ Ala Pro Val Asn Thr Thr Thr Glu Asp Glu Thr Ala Gln Ile Pro Ala Glu Ala Val

ATC GGT TAC TTA GAT TTA GAA GGG GAT TTC GAT GTT GCT GTT TTG CCA TTT TCC AAC  
TAC CCA ATG AAT CTA AAT CTT CCC CTA AAG CTA CAA CGA CAA AAC GGT AAA AGG TTG  
▶ Ile Gly Tyr Leu Asp Leu Glu Gly Asp Phe Asp Val Ala Val Leu Pro Phe Ser Asn

AGC ACA AAT AAC GGG TTA TTG TTT ATA AAT ACT ACT ATT GCC AGC ATT GCT GCT AAA  
TCG TGT TTA TTG CCC AAT AAC AAA TAT TTA TGA TGA TAA CCG TCG TAA CGA CGA TTT  
▶ Ser Thr Asn Asn Gly Leu Leu Phe Ile Asn Thr Thr Ile Ala Ser Ile Ala Ala Lys

XbaI

KPI(-4-57; M15A, I16H)

GAA GAA GGG GTA TCT CTA GAT AAA AGA GAG GTT GTT AGA GAG GTG TGC TCT GAA CAA  
CTT CTT CCC CAT AGA GAT CTA TTT TCT CTC CAA CAA TCT CTC CAC ACG AGA CTT GTT  
▶ Glu Glu Gly Val Ser Leu Asp Lys Arg Glu Val Val Arg Glu Val Cys Ser Glu Gln

RsrII

AgeI

AatII

GCT GAG ACC GGT CCG TGC CGT GCA GCT CAC TCC CGC TGG TAC TTT GAC GTC ACT GAA  
CGA CTC TGG CCA GGC ACG GCA CGT CGA GTG AGG GCG ACC ATG AAA CTG CAG TGA CTT  
▶ Ala Glu Thr Gly Pro Cys Arg Ala Ala His Ser Arg Trp Tyr Phe Asp Val Thr Glu

GGT AAG TGC GCT CCA TTC TTT TAC GGC GGT TGC GGC GGC AAC CGT AAC AAC TTT GAC  
CCA TTC ACG CGA GGT AAG AAA ATG CCG CCA ACG CCG CCG TTG GCA TTG TTG AAA CTG  
▶ Gly Lys Cys Ala Pro Phe Phe Tyr Gly Gly Cys Gly Gly Asn Arg Asn Asn Phe Asp

BamHI

HindIII

ACT GAA GAG TAC TGC ATG GCA GTG TGC GGA TCC GCT ATT TAA GCT T  
TGA CTT CTC ATG ACG TAC CGT CAC ACG CCT AGG CGA TAA ATT CGA A  
▶ Thr Glu Glu Tyr Cys Met Ala Val Cys Gly Ser Ala Ile

206720" 4099200T

Title: PROTEASE INHIBITOR  
PEPTIDES

Inventor(s): R. Tyler WHITE et al.

Appl. No.: 09/201,715

Figure 19

pTW6174

α-factor

ATG AGA TTT CCT TCA ATT TTT ACT GCA GTT TTA TTC GCA GCA TCC TCC GCA TTA GCT  
TAC TCT AAA GGA AGT TAA AAA TGA CGT CAA AAT AAG CGT CGT AGG AGG CGT AAT CGA  
▶Met Arg Phe Pro Ser Ile Phe Thr Ala Val Leu Phe Ala Ala Ser Ser Ala Leu Ala  
  
GCT CCA GTC AAC ACT ACA ACA GAA GAT GAA ACG GCA CAA ATT CCG GCT GAA GCT GTC  
CGA GGT CAG TIG TGA TGT TGT CTT CTA CTT TGC CGT GTT TAA GGC CGA CTT CGA CAG  
▶Ala Pro Val Asn Thr Thr Thr Glu Asp Glu Thr Ala Gln Ile Pro Ala Glu Ala Val  
  
ATC GGT TAC TTA GAT TTA GAA GGG GAT TTC GAT GTT GCT GTT TTG CCA TTT TCC AAC  
TAG CCA ATG AAT CTA AAT CTT CCC CTA AAG CTA CAA CGA CAA AAC GGT AAA AGG TTG  
▶Ile Gly Tyr Leu Asp Leu Glu Gly Asp Phe Asp Val Ala Val Leu Pro Phe Ser Asn  
  
AGC ACA AAT AAC GGG TTA TTG TTT ATA AAT ACT ACT ATT GCC AGC ATT GCT GCT AAA  
TCG TGT TTA TTG CCC AAT AAC AAA TAT TTA TGA TGA TAA CGG TCG TAA CGA CGA TTT  
▶Ser Thr Asn Asn Gly Leu Leu Phe Ile Asn Thr Thr Ile Ala Ser Ile Ala Ala Lys

XbaI

KPI(-4-57; M15L, I16H)

GAA GAA GGG GTA TCT CTA GAT AAA AGA GAG GTT GTT AGA GAG GTG TGC TCT GAA CAA  
CTT CTT CCC CAT AGA GAT CTA TTT TCT CTC CAA CAA TCT CTC CAC ACG AGA CTT GTT  
▶Glu Glu Gly Val Ser Leu Asp Lys Arg Glu Val Val Arg Glu Val Cys Ser Glu Gln

RsrII

AgeI

AatII

GCT GAG ACC GGT CCG TGC CGT GCA TTG CAC TCC CGC TGG TAC TTT GAC GTC ACT GAA  
CGA CTC TGG CCA GGC ACG GCA CGT AAC GTG AGG GCG ACC ATG AAA CTG CAG TGA CTT  
▶Ala Glu Thr Gly Pro Cys Arg Ala Leu His Ser Arg Trp Tyr Phe Asp Val Thr Glu  
  
GGT AAG TGC GCT CCA TTC TTT TAC GGC GGT TGC GGC GGC AAC CGT AAC AAC TTT GAC  
CCA TTC ACG CGA GGT AAG AAA ATG CCG CCA ACG CCG CCG TTG GCA TTG TTG AAA CTG  
▶Gly Lys Cys Ala Pro Phe Phe Tyr Gly Gly Cys Gly Gly Asn Arg Asn Asn Phe Asp

BamHI

HindIII

ACT GAA GAG TAC TGC ATG GCA GTG TGC GGA TCC GCT ATT TAA GCT T  
TGA CTT CTC ATG ACG TAC CGT CAC ACG CCT AGG CGA TAA ATT CGA A  
▶Thr Glu Glu Tyr Cys Met Ala Val Cys Gly Ser Ala Ile

20075604-021902

Title: PROTEASE INHIBITOR  
PEPTIDES  
Inventor(s): R. Tyler WHITE et al.  
Appl. No.: 09/201,715

Figure 20

KPI(-4-57; M15A, S17W) TW6165

Glu - Val - Val - Arg - Glu - Val - Cys - Ser - Glu - Gln - Ala  
-4 -3 -2 -1 1 2 3 4 5 6 7

Glu - Thr - Gly - Pro - Cys - Arg - Ala - Ala - Ile - Trp - Arg  
8 9 10 11 12 13 14 15 16 17 18

Trp - Tyr - Phe - Asp - Val - Thr - Glu - Gly - Lys - Cys - Ala  
19 20 21 22 23 24 25 26 27 28 29

Pro - Phe - Phe - Tyr - Gly - Gly - Cys - Gly - Gly - Asn - Arg  
30 31 32 33 34 35 36 37 38 39 40

Asn - Asn - Phe - Asp - Thr - Glu - Glu - Tyr - Cys - Met - Ala  
41 42 43 44 45 46 47 48 49 50 51

Val - Cys - Gly - Ser - Ala - Ile  
52 53 54 55 56 57

10076604.021902

Figure 21

KPI(-4-57; M15A, S17Y) TW6166

Glu - Val - Val - Arg - Glu - Val - Cys - Ser - Glu - Gln - Ala  
-4 -3 -2 -1 1 2 3 4 5 6 7

Glu - Thr - Gly - Pro - Cys - Arg - Ala - Ala - Ile - Tyr - Arg  
8 9 10 11 12 13 14 15 16 17 18

Trp - Tyr - Phe - Asp - Val - Thr - Glu - Gly - Lys - Cys - Ala  
19 20 21 22 23 24 25 26 27 28 29

Pro - Phe - Phe - Tyr - Gly - Gly - Cys - Gly - Gly - Asn - Arg  
30 31 32 33 34 35 36 37 38 39 40

Asn - Asn - Phe - Asp - Thr - Glu - Glu - Tyr - Cys - Met - Ala  
41 42 43 44 45 46 47 48 49 50 51

Val - Cys - Gly - Ser - Ala - Ile  
52 53 54 55 56 57

206720-10992001

Figure 22

KPI(-4-57; M15L, S17F) TW6175

Glu - Val - Val - Arg - Glu - Val - Cys - Ser - Glu - Gln - Ala  
-4 -3 -2 -1 1 2 3 4 5 6 7

Glu - Thr - Gly - Pro - Cys - Arg - Ala - Leu - Ile - Phe - Arg  
8 9 10 11 12 13 14 15 16 17 18

Trp - Tyr - Phe - Asp - Val - Thr - Glu - Gly - Lys - Cys - Ala  
19 20 21 22 23 24 25 26 27 28 29

Pro - Phe - Phe - Tyr - Gly - Gly - Cys - Gly - Gly - Asn - Arg  
30 31 32 33 34 35 36 37 38 39 40

Asn - Asn - Phe - Asp - Thr - Glu - Glu - Tyr - Cys - Met - Ala  
41 42 43 44 45 46 47 48 49 50 51

Val - Cys - Gly - Ser - Ala - Ile  
52 53 54 55 56 57

2007604-021902

Figure 23

KPI(-4-57; M15L, S17Y) BG028

Glu - Val - Val - Arg - Glu - Val - Cys - Ser - Glu - Gln - Ala  
-4 -3 -2 -1 1 2 3 4 5 6 7

Glu - Thr - Gly - Pro - Cys - Arg - Ala - Leu - Ile - Tyr - Arg  
8 9 10 11 12 13 14 15 16 17 18

Trp - Tyr - Phe - Asp - Val - Thr - Glu - Gly - Lys - Cys - Ala  
19 20 21 22 23 24 25 26 27 28 29

Pro - Phe - Phe - Tyr - Gly - Gly - Cys - Gly - Gly - Asn - Arg  
30 31 32 33 34 35 36 37 38 39 40

Asn - Asn - Phe - Asp - Thr - Glu - Glu - Tyr - Cys - Met - Ala  
41 42 43 44 45 46 47 48 49 50 51

Val - Cys - Gly - Ser - Ala - Ile  
52 53 54 55 56 57

1007604.021902

Title: PROTEASE INHIBITOR  
PEPTIDES  
Inventor(s): R. Tyler WHITE et al.  
Appl. No.: 09/201,715

Figure 24

KPI(-4-57; I16H, S17F) TW6183

Glu - Val - Val - Arg - Glu - Val - Cys - Ser - Glu - Gln - Ala  
-4 -3 -2 -1 1 2 3 4 5 6 7

Glu - Thr - Gly - Pro - Cys - Arg - Ala - Met - His - Phe - Arg  
8 9 10 11 12 13 14 15 16 17 18

Trp - Tyr - Phe - Asp - Val - Thr - Glu - Gly - Lys - Cys - Ala  
19 20 21 22 23 24 25 26 27 28 29

Pro - Phe - Phe - Tyr - Gly - Gly - Cys - Gly - Gly - Asn - Arg  
30 31 32 33 34 35 36 37 38 39 40

Asn - Asn - Phe - Asp - Thr - Glu - Glu - Tyr - Cys - Met - Ala  
41 42 43 44 45 46 47 48 49 50 51

Val - Cys - Gly - Ser - Ala - Ile  
52 53 54 55 56 57

10076604-021902



Title: PROTEASE INHIBITOR  
PEPTIDES  
Inventor(s): R. Tyler WHITE et al.  
Appl. No.: 09/201,715

Figure 25

KPI(-4-57; I16H, S17Y) TW6184

Glu - Val - Val - Arg - Glu - Val - Cys - Ser - Glu - Gln - Ala  
-4 -3 -2 -1 1 2 3 4 5 6 7

Glu - Thr - Gly - Pro - Cys - Arg - Ala - Met - His - Tyr - Arg  
8 9 10 11 12 13 14 15 16 17 18

Trp - Tyr - Phe - Asp - Val - Thr - Glu - Gly - Lys - Cys - Ala  
19 20 21 22 23 24 25 26 27 28 29

Pro - Phe - Phe - Tyr - Gly - Gly - Cys - Gly - Gly - Asn - Arg  
30 31 32 33 34 35 36 37 38 39 40

Asn - Asn - Phe - Asp - Thr - Glu - Glu - Tyr - Cys - Met - Ala  
41 42 43 44 45 46 47 48 49 50 51

Val - Cys - Gly - Ser - Ala - Ile  
52 53 54 55 56 57

20070604-021902

Title: PROTEASE INHIBITOR  
PEPTIDES  
Inventor(s): R. Tyler WHITE et al.  
Appl. No.: 09/201,715

Figure 26

KPI(-4-57; I16H, S17W) TW6185

Glu - Val - Val - Arg - Glu - Val - Cys - Ser - Glu - Gln - Ala  
-4 -3 -2 -1 1 2 3 4 5 6 7

Glu - Thr - Gly - Pro - Cys - Arg - Ala - Met - His - Trp - Arg  
8 9 10 11 12 13 14 15 16 17 18

Trp - Tyr - Phe - Asp - Val - Thr - Glu - Gly - Lys - Cys - Ala  
19 20 21 22 23 24 25 26 27 28 29

Pro - Phe - Phe - Tyr - Gly - Gly - Cys - Gly - Gly - Asn - Arg  
30 31 32 33 34 35 36 37 38 39 40

Asn - Asn - Phe - Asp - Thr - Glu - Glu - Tyr - Cys - Met - Ala  
41 42 43 44 45 46 47 48 49 50 51

Val - Cys - Gly - Ser - Ala - Ile  
52 53 54 55 56 57

20076604-024902

Title: PROTEASE INHIBITOR  
PEPTIDES  
Inventor(s): R. Tyler WHITE et al.  
Appl. No.: 09/201,715

Figure 27

KPI(-4-57; M15A, S17F) DD185

Glu - Val - Val - Arg - Glu - Val - Cys - Ser - Glu - Gln - Ala  
-4 -3 -2 -1 1 2 3 4 5 6 7

Glu - Thr - Gly - Pro - Cys - Arg - Ala - Ala - Ile - Phe - Arg  
8 9 10 11 12 13 14 15 16 17 18

Trp - Tyr - Phe - Asp - Val - Thr - Glu - Gly - Lys - Cys - Ala  
19 20 21 22 23 24 25 26 27 28 29

Pro - Phe - Phe - Tyr - Gly - Gly - Cys - Gly - Gly - Asn - Arg  
30 31 32 33 34 35 36 37 38 39 40

Asn - Asn - Phe - Asp - Thr - Glu - Glu - Tyr - Cys - Met - Ala  
41 42 43 44 45 46 47 48 49 50 51

Val - Cys - Gly - Ser - Ala - Ile  
52 53 54 55 56 57

20076604-021902

Title: PROTEASE INHIBITOR  
PEPTIDES

Inventor(s): R. Tyler WHITE et al.

Appl. No.: 09/201,715

Figure 28

KPI(-4-57; M15A, I16H) TW6173

Glu - Val - Val - Arg - Glu - Val - Cys - Ser - Glu - Gln - Ala  
-4 -3 -2 -1 1 2 3 4 5 6 7

Glu - Thr - Gly - Pro - Cys - Arg - Ala - Ala - His - SerTrp - Arg  
8 9 10 11 12 13 14 15 16 17 18

Trp - Tyr - Phe - Asp - Val - Thr - Glu - Gly - Lys - Cys - Ala  
19 20 21 22 23 24 25 26 27 28 29

Pro - Phe - Phe - Tyr - Gly - Gly - Cys - Gly - Gly - Asn - Arg  
30 31 32 33 34 35 36 37 38 39 40

Asn - Asn - Phe - Asp - Thr - Glu - Glu - Tyr - Cys - Met - Ala  
41 42 43 44 45 46 47 48 49 50 51

Val - Cys - Gly - Ser - Ala - Ile  
52 53 54 55 56 57

20075604-021902

Figure 29

KPI(-4-57; M15L, I16H) TW6174

Glu - Val - Val - Arg - Glu - Val - Cys - Ser - Glu - Gln - Ala  
-4 -3 -2 -1 1 2 3 4 5 6 7

Glu - Thr - Gly - Pro - Cys - Arg - Ala - Leu - His - Ser - Arg  
8 9 10 11 12 13 14 15 16 17 18

Trp - Tyr - Phe - Asp - Val - Thr - Glu - Gly - Lys - Cys - Ala  
19 20 21 22 23 24 25 26 27 28 29

Pro - Phe - Phe - Tyr - Gly - Gly - Cys - Gly - Gly - Asn - Arg  
30 31 32 33 34 35 36 37 38 39 40

Asn - Asn - Phe - Asp - Thr - Glu - Glu - Tyr - Cys - Met - Ala  
41 42 43 44 45 46 47 48 49 50 51

Val - Cys - Gly - Ser - Ala - Ile  
52 53 54 55 56 57

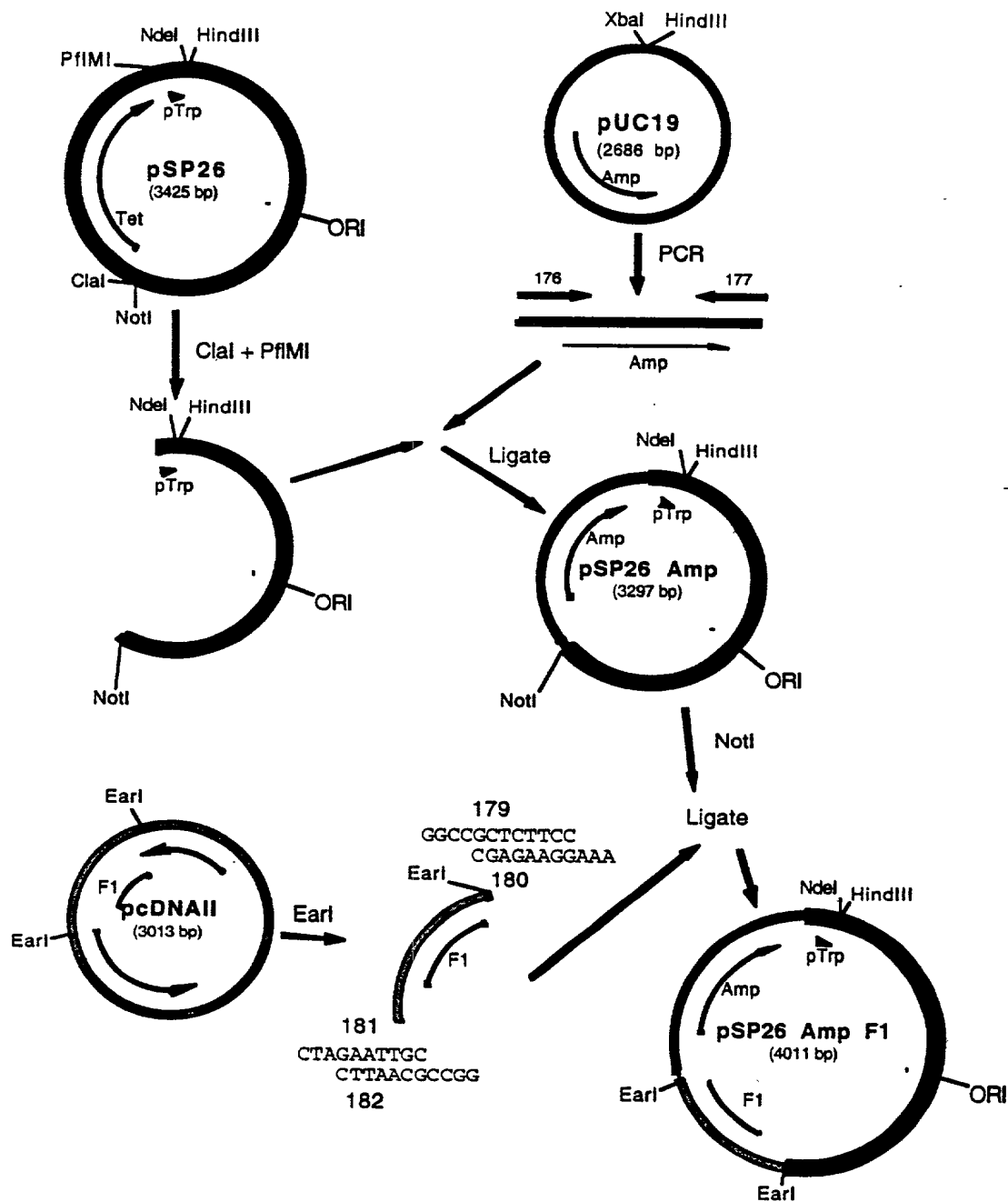
2006T20-4099Z001

Title: PROTEASE INHIBITOR  
PEPTIDES

Inventor(s): R. Tyler WHITE et al.

Appl. No.: 09/201,715

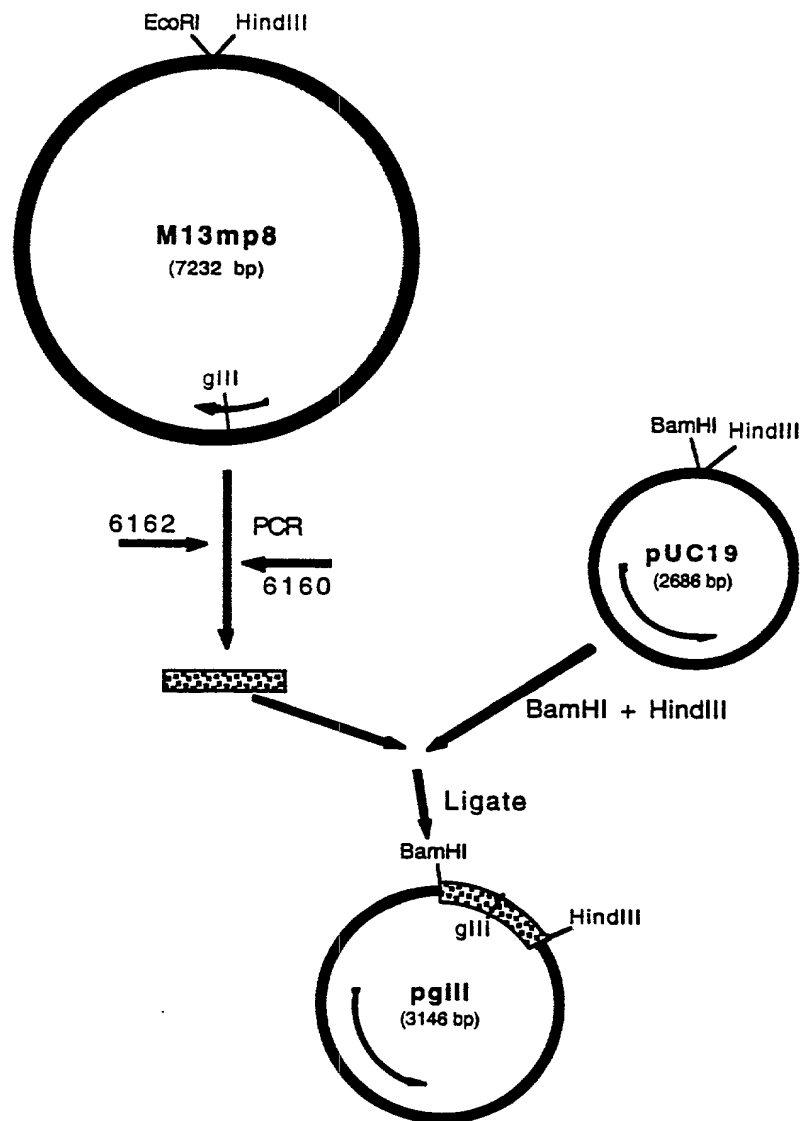
Figure 30



Title: PROTEASE INHIBITOR  
PEPTIDES

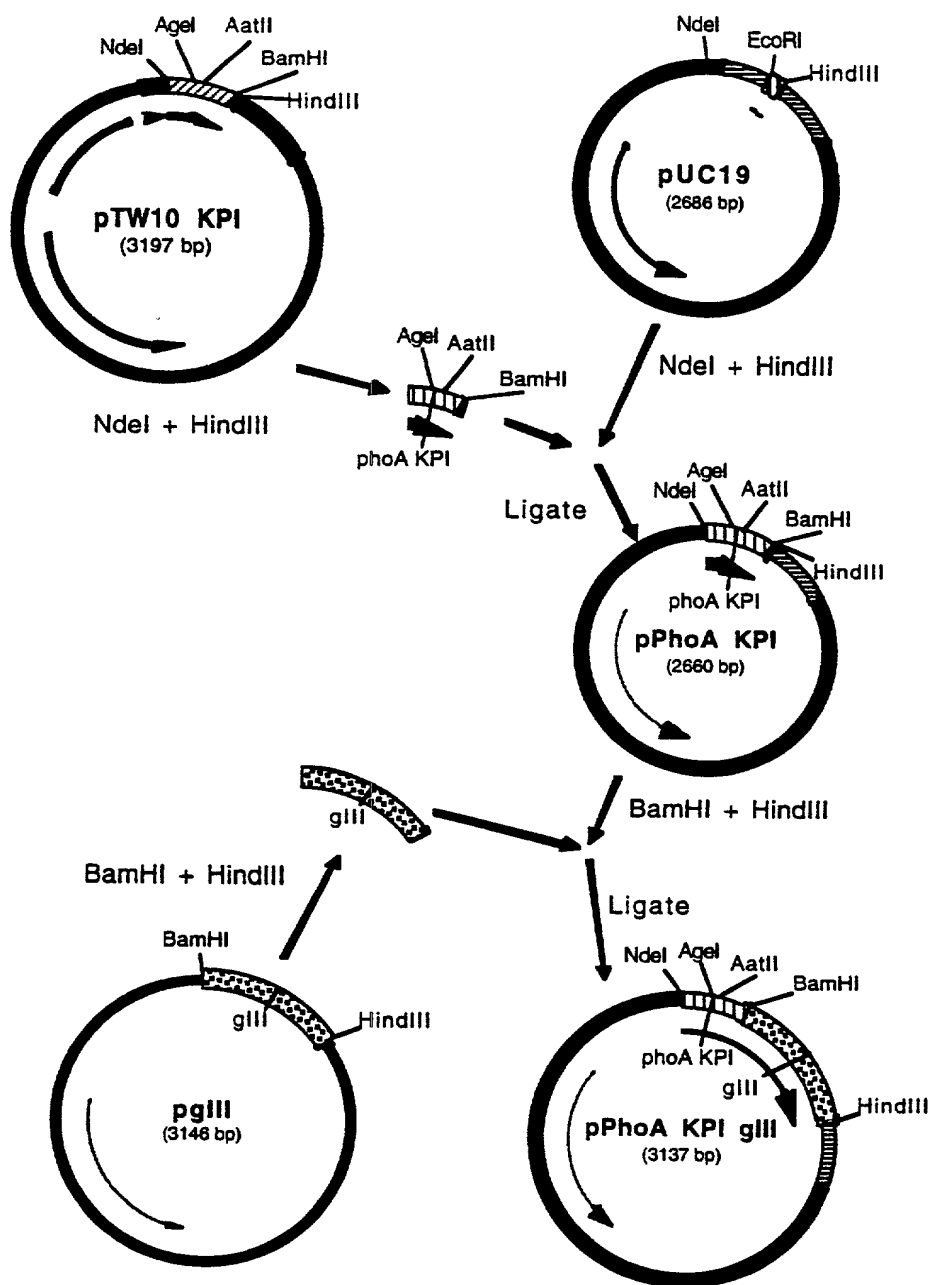
Inventor(s): R. Tyler WHITE et al.  
Appl. No.: 09/201,715

Figure 31



206720-40992001

Figure 32



20070604-024902

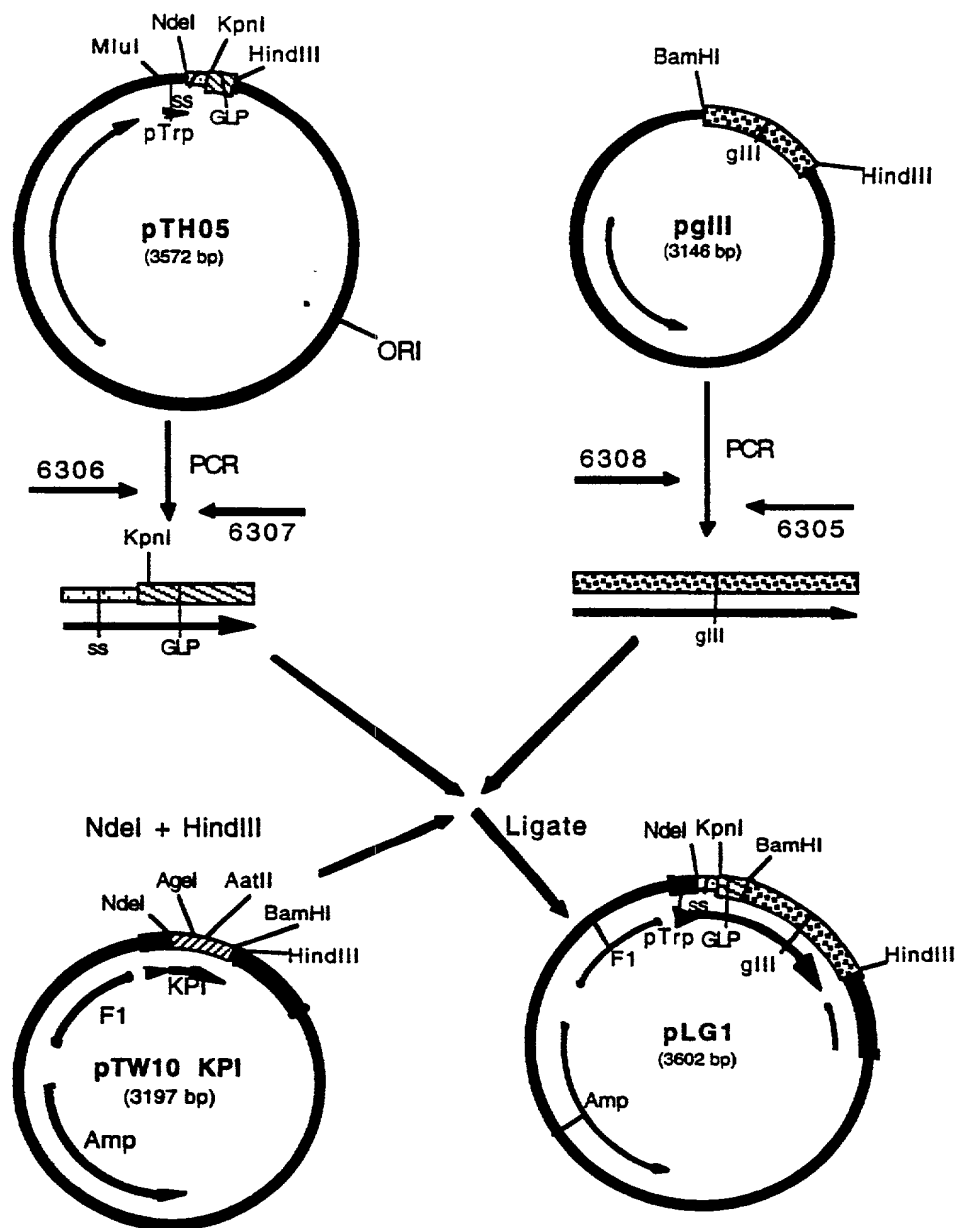


Title: PROTEASE INHIBITOR  
PEPTIDES

Inventor(s): R. Tyler WHITE et al.

Appl. No.: 09/201,715

Figure 33



20070604-0300

Title: PROTEASE INHIBITOR  
PEPTIDES

Inventor(s): R. Tyler WHITE et al.

Appl. No.: 09/201,715

Figure 34

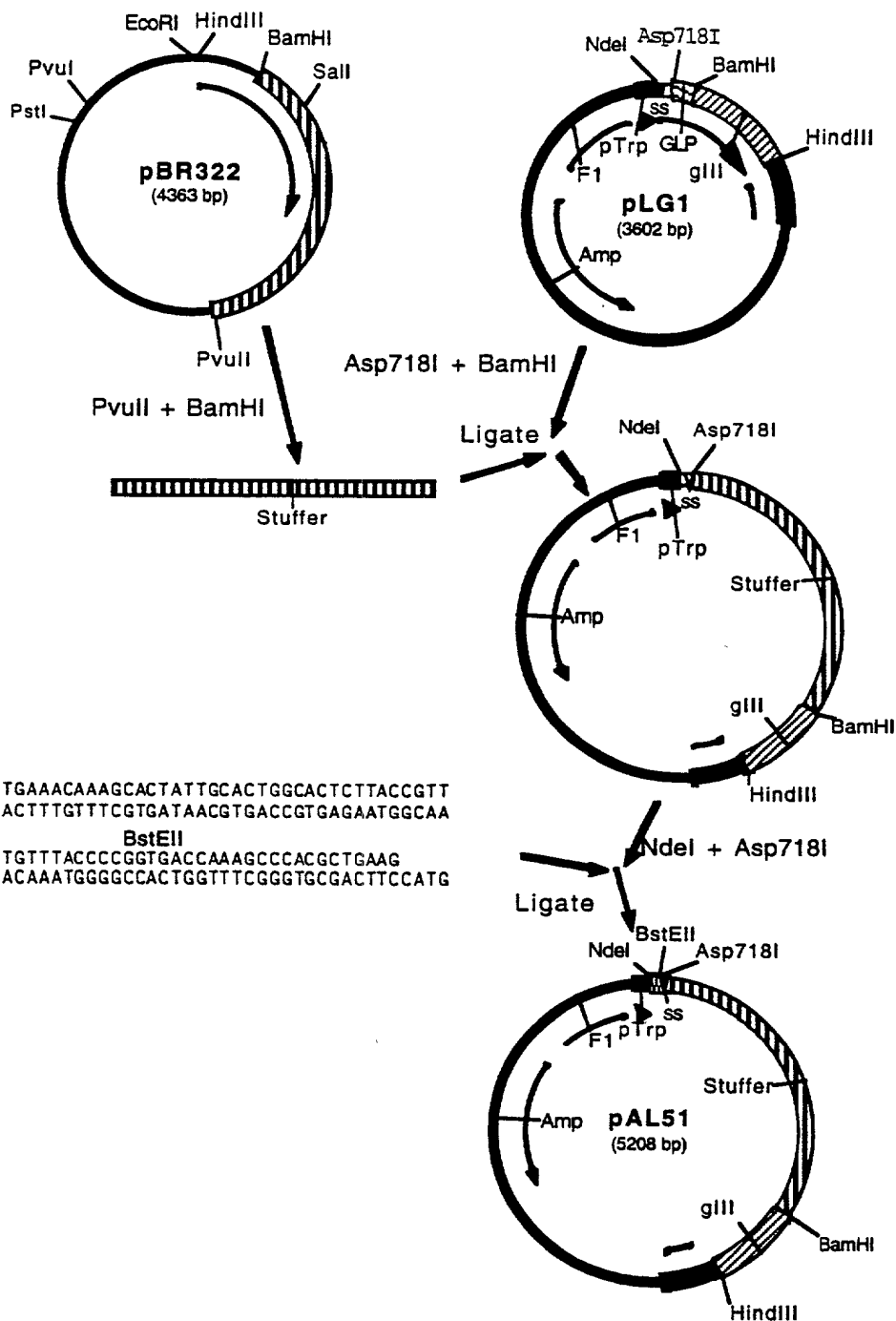


Figure 35

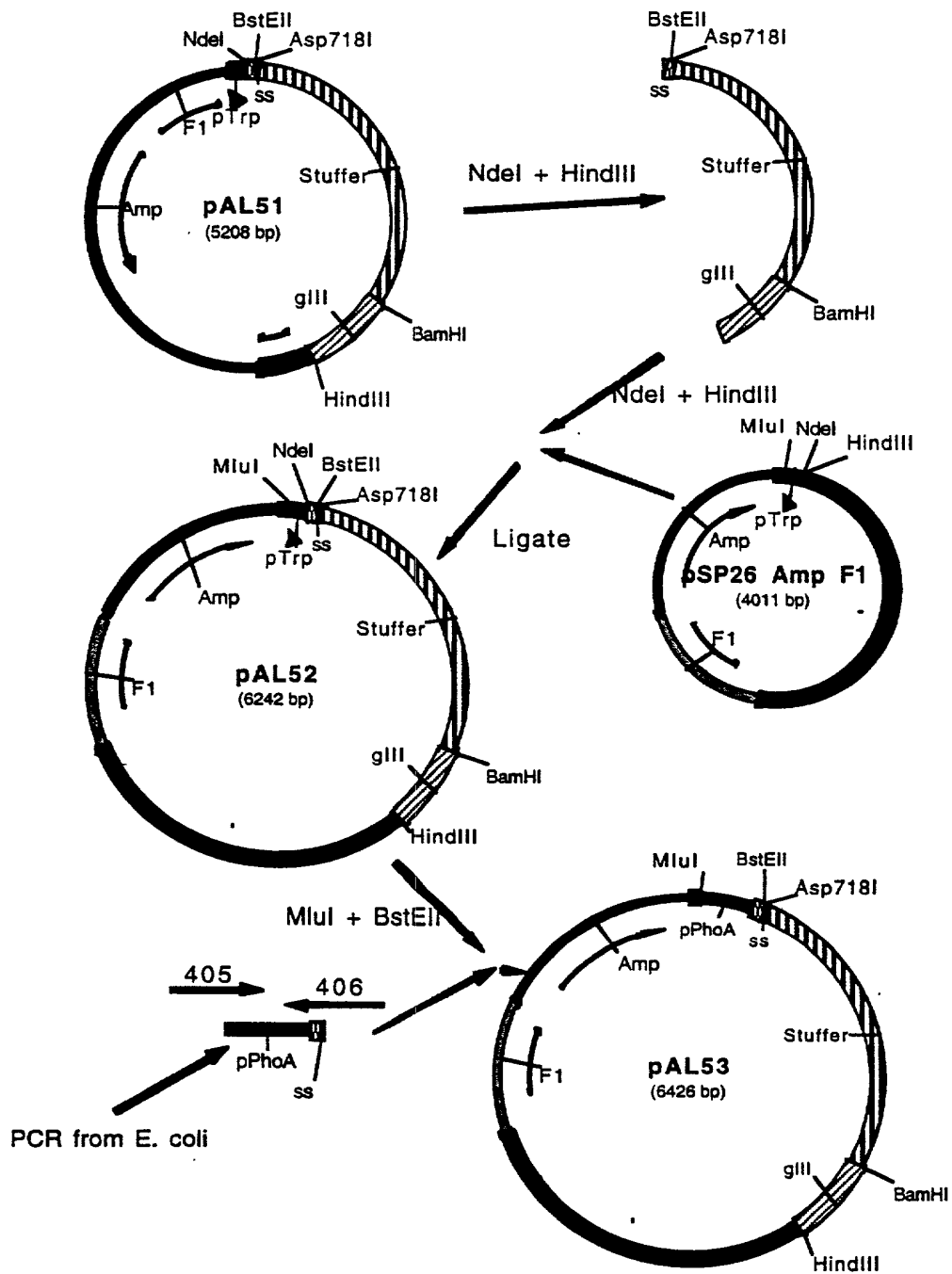
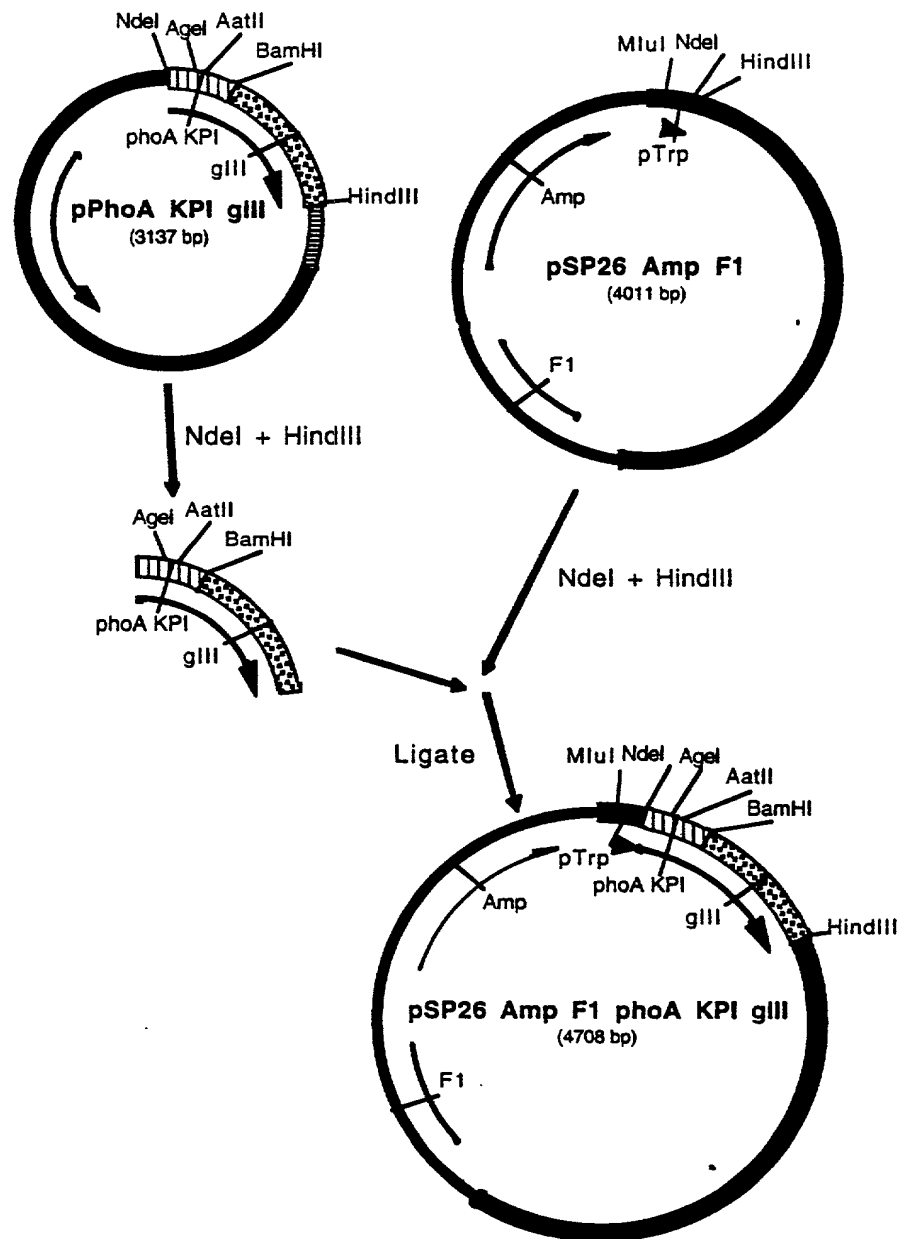
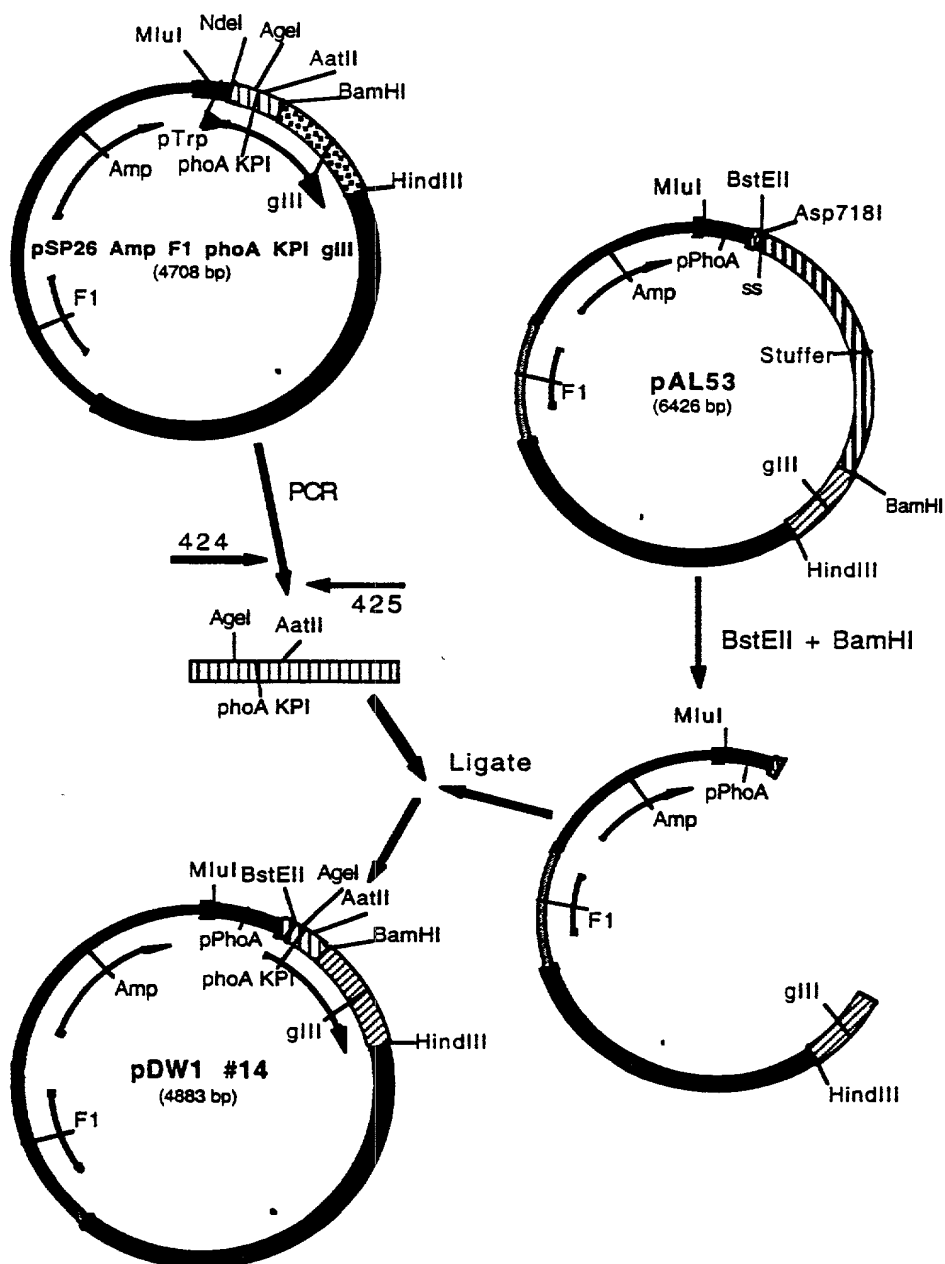


Figure 36



20076604-021902

Figure 37



206T20-4099Z001

Title: PROTEASE INHIBITOR  
PEPTIDES

Inventor(s): R. Tyler WHITE et al.

Appl. No.: 09/201,715

Figure 38

phoA signal →

GTG AAA CAA AGC ACT ATT GCA CTG GCA CTC TTA CCG TTA CTG TTT ACC CCG GTG ACC AAA  
▶ Val Lys Gln Ser Thr Ile Ala Leu Ala Leu Leu Pro Leu Leu Phe Thr Pro Val Thr Lys

BstEII

KPI (1-55) →

GCC GAG GTG TGC TCT GAA CAA GCT GAG ACC GGT CCG TGC CGT GCA ATG ATC TCC CGC TGG  
▶ Ala Glu Val Cys Ser Glu Gln Ala Glu Thr Gly Pro Cys Arg Ala Met Ile Ser Arg Trp

AgeI

AatII

TAC TTT GAC GTC ACT GAA GGT AAG TGC GCT CCA TTC TTT TAC GGC GGT TGC GGC GGC AAC  
▶ Tyr Phe Asp Val Thr Glu Gly Lys Cys Ala Pro Phe Phe Tyr Gly Gly Cys Gly Gly Asn

BamHI

gIII →

CGT AAC AAC TTT GAC ACT GAA GAG TAC TGC ATG GCA GTG TGC GGA TCC GGT GGT GGC TCT  
▶ Arg Asn Asn Phe Asp Thr Glu Glu Tyr Cys Met Ala Val Cys Gly Ser Gly Gly Gly Ser

GGT TCC GGT GAT TTT GAT TAT GAA AAG ATG GCA AAC GCT AAT AAG GGG GCT ATG ACC GAA  
▶ Gly Ser Gly Asp Phe Asp Tyr Glu Lys Met Ala Asn Ala Asn Lys Gly Ala Met Thr Glu

AAT GCC GAT GAA AAC GCG CTA CAG TCT GAC GCT AAA GGC AAA CTT GAT TCT GTC GCT ACT  
▶ Asn Ala Asp Glu Asn Ala Leu Gln Ser Asp Ala Lys Gly Lys Leu Asp Ser Val Ala Thr

GAT TAC GGT GCT GCT ATC GAT GGT TTC ATT GGT GAC GTT TCC GGC CTT GCT AAT GGT AAT  
▶ Asp Tyr Gly Ala Ala Ile Asp Gly Phe Ile Gly Asp Val Ser Gly Leu Ala Asn Gly Asn

GGT GCT ACT GGT GAT TTT GCT GGC TCT AAT TCC CAA ATG GCT CAA GTC GGT GAC GGT GAT  
▶ Gly Ala Thr Gly Asp Phe Ala Gly Ser Asn Ser Gln Met Ala Gln Val Gly Asp Gly Asp

AAT TCA CCT TTA ATG AAT AAT TTC CGT CAA TAT TTA CCT TCC CTC CCT CAA TCG GTT GAA  
▶ Asn Ser Pro Leu Met Asn Asn Phe Arg Gln Tyr Leu Pro Ser Leu Pro Gln Ser Val Glu

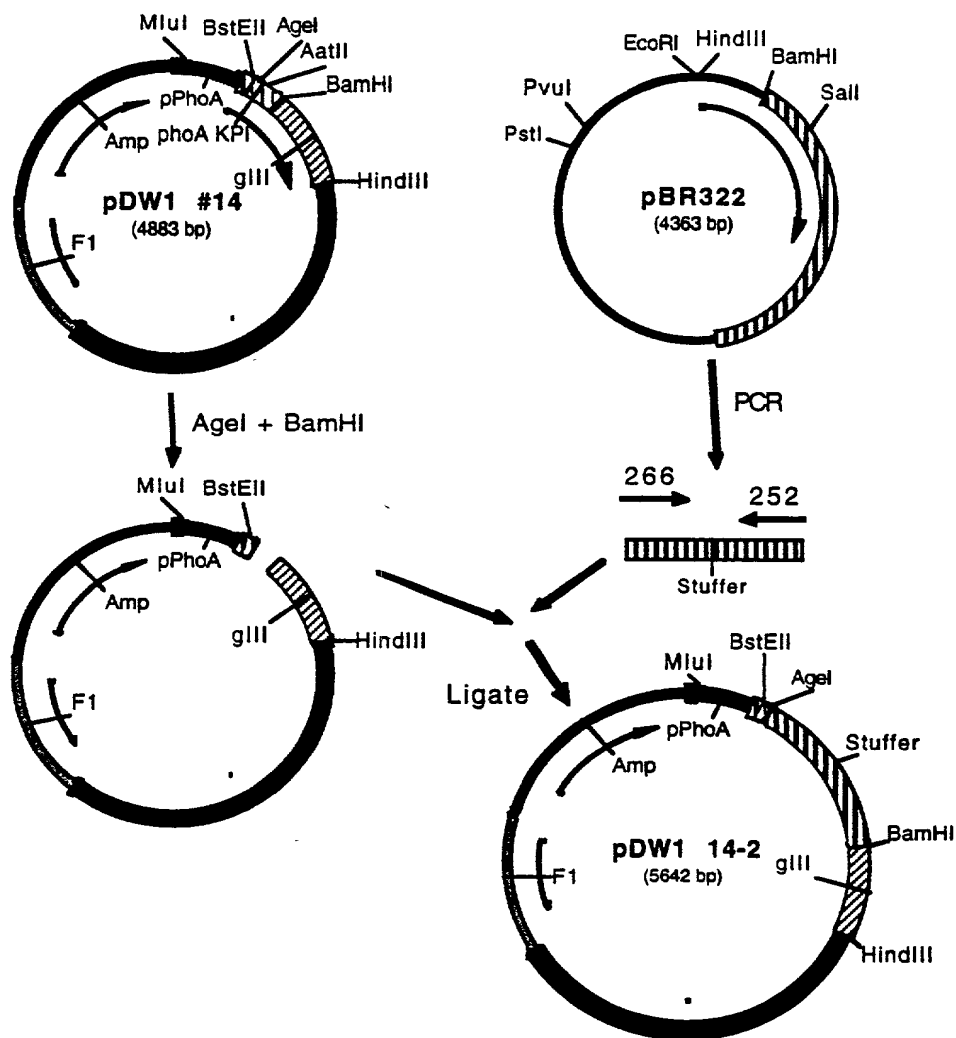
TGT CGC CCT TTT GTC TTT GGC GCT GGT AAA CCA TAC GAA TTT TCT ATT GAT TGT GAC AAA  
▶ Cys Arg Pro Phe Val Phe Gly Ala Gly Lys Pro Tyr Glu Phe Ser Ile Asp Cys Asp Lys

ATA AAC TTA TTC CGT GGT GTC TTT GCG TTT CTT TTA TAT GTT GCC ACC TTT ATG TAT GTA  
▶ Ile Asn Leu Phe Arg Gly Val Phe Ala Phe Leu Leu Tyr Val Ala Thr Phe Met Tyr Val

TTT TCT ACG TTT GCT AAC ATA CTG CGT AAT AAG GAG TCT TAA TA  
▶ Phe Ser Thr Phe Ala Asn Ile Leu Arg Asn Lys Glu Ser ...

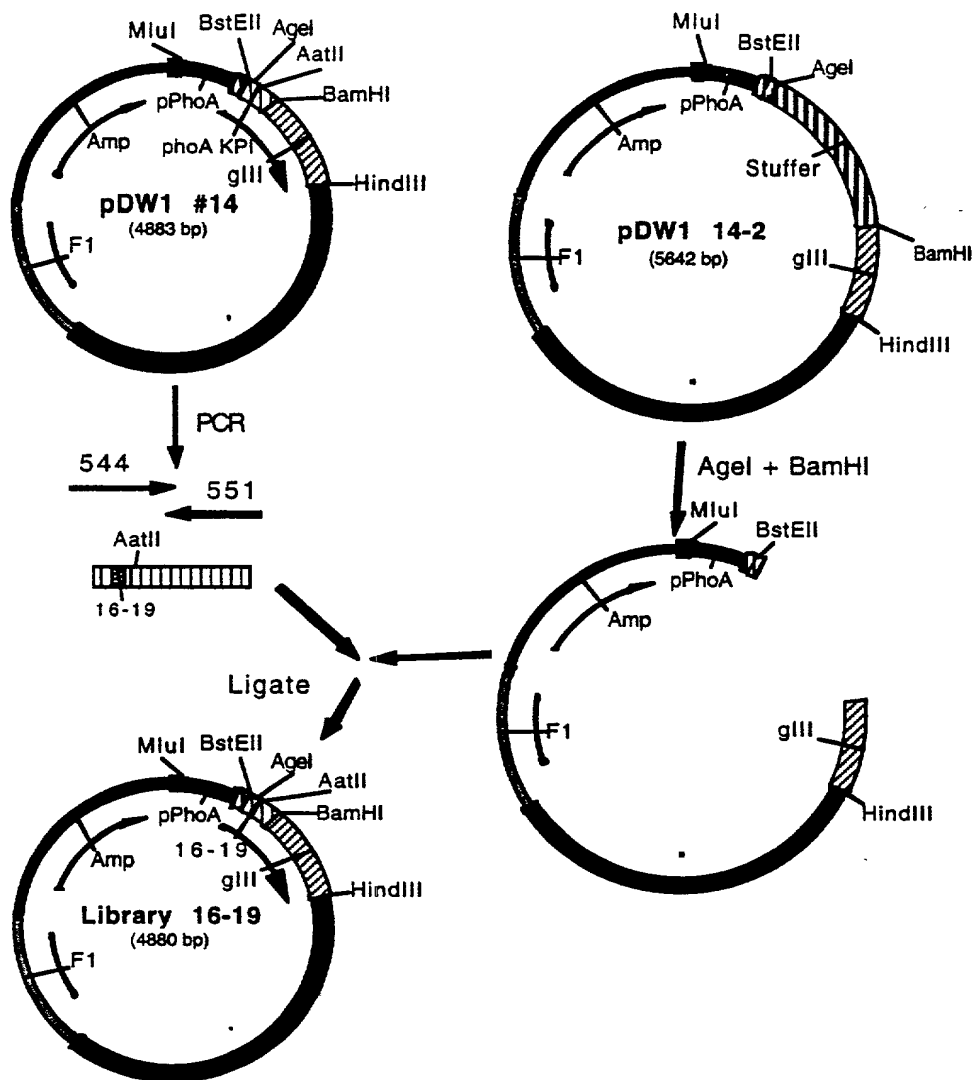
10076604-021902

Figure 39



20070504-021902

Figure 40





## Title: PROTEASE INHIBITOR

## PEPTIDES

Inventor(s): R. Tyler WHITE et al.

Appl. No.: 09/201,715

Figure 41

phoA signal →

GTG AAA CAA AGC ACT ATT GCA CTG GCA CTC TTA CCG TTA CTG TTT ACC CCG GTG ACC AAA  
 ▶ Val Lys Gln Ser Thr Ile Ala Leu Ala Leu Leu Pro Leu Leu Phe Thr Pro Val Thr Lys

BstEII

KPI (1-55; 16 - 19) → Agel 16 - 19

GCC GAG GTG TGC TCT GAA CAA GCT GAG ACC GGT CCG TGC CGT NNS NNS NNS NNS TGG TAC  
 ▶ Ala Glu Val Cys Ser Glu Gln Ala Glu Thr Gly Pro Cys Arg --- --- --- --- Trp Tyr

AatII

TTT GAC GTC ACT GAA GGT AAG TGC GCT CCA TTC TTT TAC GGC GGT TGC GGC GGC AAC CGT  
 ▶ Phe Asp Val Thr Glu Gly Lys Cys Ala Pro Phe Phe Tyr Gly Gly Cys Gly Asn Arg

BamHI gIII

AAC AAC TTT GAC ACT GAA GAG TAC TGC ATG GCA GTG TGC GGA TCC GGT GGT GGC TCT GGT  
 ▶ Asn Asn Phe Asp Thr Glu Glu Tyr Cys Met Ala Val Cys Gly Ser Gly Gly Gly Ser Gly

TCC GGT GAT TTT GAT TAT GAA AAG ATG GCA AAC GCT AAT AAG GGG GCT ATG ACC GAA AAT  
 ▶ Ser Gly Asp Phe Asp Tyr Glu Lys Met Ala Asn Ala Asn Lys Gly Ala Met Thr Glu Asn

GCC GAT GAA AAC GCG CTA CAG TCT GAC GCT AAA GGC AAA CTT GAT TCT GTC GCT ACT GAT  
 ▶ Ala Asp Glu Asn Ala Leu Gln Ser Asp Ala Lys Gly Lys Leu Asp Ser Val Ala Thr Asp

TAC GGT GCT GCT ATC GAT GGT TTC ATT GGT GAC GTT TCC GGC CTT GCT AAT GGT AAT GGT  
 ▶ Tyr Gly Ala Ala Ile Asp Gly Phe Ile Gly Asp Val Ser Gly Leu Ala Asn Gly Asn Gly

gIII

GCT ACT GGT GAT TTT GCT GGC TCT AAT TCC CAA ATG GCT CAA GTC GGT GAC GGT GAT AAT  
 ▶ Ala Thr Gly Asp Phe Ala Gly Ser Asn Ser Gln Met Ala Gln Val Gly Asp Gly Asp Asn

TCA CCT TTA ATG AAT AAT TTC CGT CAA TAT TTA CCT TCC CTC CCT CAA TCG GTT GAA TGT  
 ▶ Ser Pro Leu Met Asn Asn Phe Arg Gln Tyr Leu Pro Ser Leu Pro Gln Ser Val Glu Cys

CGC CCT TTT GTC TTT GGC GCT GGT AAA CCA TAC GAA TTT TCT ATT GAT TGT GAC AAA ATA  
 ▶ Arg Pro Phe Val Phe Gly Ala Gly Lys Pro Tyr Glu Phe Ser Ile Asp Cys Asp Lys Ile

AAC TTA TTC CGT GGT GTC TTT GCG TTT CTT TTA TAT GTT GCC ACC TTT ATG TAT GTA TTT  
 ▶ Asn Leu Phe Arg Gly Val Phe Ala Phe Leu Leu Tyr Val Ala Thr Phe Met Tyr Val Phe

TCT ACG TTT GCT AAC ATA CTG CGT AAT AAG GAG TCT TAA TA  
 ▶ Ser Thr Phe Ala Asn Ile Leu Arg Asn Lys Glu Ser ...

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Title: PROTEASE INHIBITOR  
PEPTIDES

Inventor(s): R. Tyler WHITE et al.

Appl. No.: 09/201,715

Figure 42

phoA signal →

GTG AAA CAA AGC ACT ATT GCA CTG GCA CTC TTA CCG TTA CTG TTT ACC CCG GTG ACC AAA  
▶ Val Lys Gln Ser Thr Ile Ala Leu Ala Leu Leu Pro Leu Leu Phe Thr Pro Val Thr Lys

KPI (1-55; M15A, S17F)

Agel →

GCC GAG GTG TGC TCT GAA CAA GCT GAG ACC GGT CCG TGC CGT GCA GCT ATC TTC CGC TGG  
▶ Ala Glu Val Cys Ser Glu Gln Ala Glu Thr Gly Pro Cys Arg Ala Ala Ile Phe Arg Trp

AatII →

TAC TTT GAC GTC ACT GAA GGT AAG TGC GCT CCA TTC TTT TAC GGC GGT TGC GGC GGC AAC  
▶ Tyr Phe Asp Val Thr Glu Gly Lys Cys Ala Pro Phe Phe Tyr Gly Gly Cys Gly Gly Asn

BamHI → gIII →

CGT AAC AAC TTT GAC ACT GAA GAG TAC TGC ATG GCA GTG TGC GGA TCC GGT GGT GGC TCT  
▶ Arg Asn Asn Phe Asp Thr Glu Glu Tyr Cys Met Ala Val Cys Gly Ser Gly Gly Gly Ser

GGT TCC GGT GAT TTT GAT TAT GAA AAG ATG GCA AAC GCT AAT AAG GGG GCT ATG ACC GAA  
▶ Gly Ser Gly Asp Phe Asp Tyr Glu Lys Met Ala Asn Ala Asn Lys Gly Ala Met Thr Glu

AAT GCC GAT GAA AAC GCG CTA CAG TCT GAC GCT AAA GGC AAA CTT GAT TCT GTC GCT ACT  
▶ Asn Ala Asp Glu Asn Ala Leu Gln Ser Asp Ala Lys Gly Lys Leu Asp Ser Val Ala Thr

GAT TAC GGT GCT GCT ATC GAT GGT TTC ATT GGT GAC GTT TCC GGC CTT GCT AAT GGT AAT  
▶ Asp Tyr Gly Ala Ala Ile Asp Gly Phe Ile Gly Asp Val Ser Gly Leu Ala Asn Gly Asn

GGT GCT ACT GGT GAT TTT GCT GGC TCT AAT TCC CAA ATG GCT CAA GTC GGT GAC GGT GAT  
▶ Gly Ala Thr Gly Asp Phe Ala Gly Ser Asn Ser Gln Met Ala Gln Val Gly Asp Gly Asp

AAT TCA CCT TTA ATG AAT AAT TTC CGT CAA TAT TTA CCT TCC CTC CCT CAA TCG GTT GAA  
▶ Asn Ser Pro Leu Met Asn Asn Phe Arg Gln Tyr Leu Pro Ser Leu Pro Gln Ser Val Glu

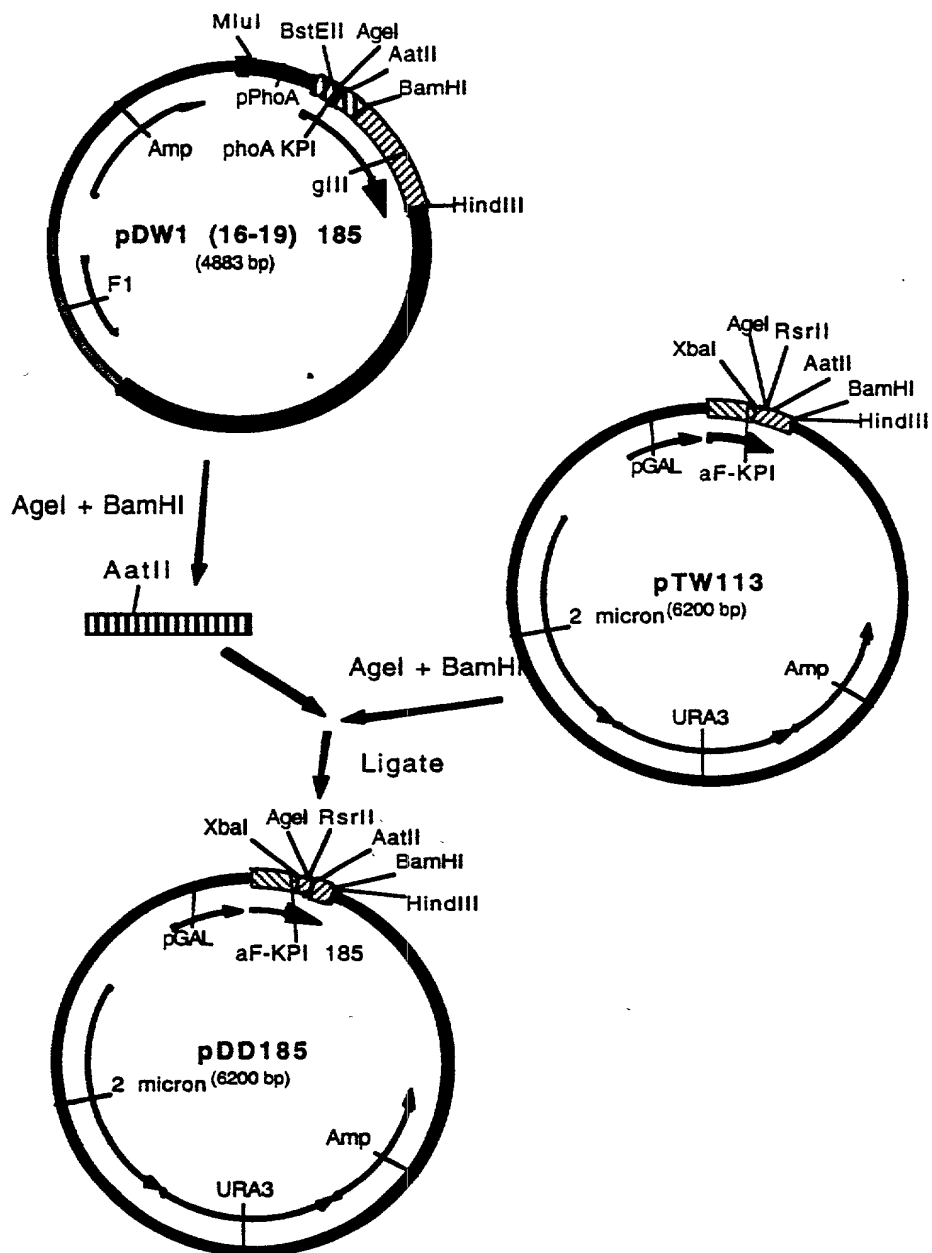
TGT CGC CCT TTT GTC TTT GGC GCT GGT AAA CCA TAC GAA TTT TCT ATT GAT TGT GAC AAA  
▶ Cys Arg Pro Phe Val Phe Gly Ala Gly Lys Pro Tyr Glu Phe Ser Ile Asp Cys Asp Lys

ATA AAC TTA TTC CGT GGT GTC TTT GCG TTT CTT TTA TAT GTT GCC ACC TTT ATG TAT GTA  
▶ Ile Asn Leu Phe Arg Gly Val Phe Ala Phe Leu Leu Tyr Val Ala Thr Phe Met Tyr Val

TTT TCT ACG TTT GCT AAC ATA CTG CGT AAT AAG GAG TCT TAA TA  
▶ Phe Ser Thr Phe Ala Asn Ile Leu Arg Asn Lys Glu Ser

10076604-021902

Figure 43



## Title: PROTEASE INHIBITOR

## PEPTIDES

Inventor(s): R. Tyler WHITE et al.

Appl. No.: 09/201,715

Figure 44

pDD185

 $\alpha$ -factor

ATG AGA TTT CCT TCA ATT TTT ACT GCA GTT TTA TTC GCA GCA TCC TCC GCA TTA GCT  
TAC TCT AAA GGA AGT TAA AAA TGA CGT CAA AAT AAG CGT CGT AGG AGG CGT AAT CGA  
▶ Met Arg Phe Pro Ser Ile Phe Thr Ala Val Leu Phe Ala Ala Ser Ser Ala Leu Ala  
  
GCT CCA GTC AAC ACT ACA ACA GAA GAT GAA ACG GCA CAA ATT CCG GCT GAA GCT GTC  
CGA GGT CAG TTG TGA TGT TGT CTT CTA CTT TGC CGT GTT TAA GGC CGA CTT CGA CAG  
▶ Ala Pro Val Asn Thr Thr Thr Glu Asp Glu Thr Ala Gln Ile Pro Ala Glu Ala Val  
  
ATC GGT TAC TTA GAT TTA GAA GGG GAT TTC GAT GTT GCT GTT TTG CCA TTT TCC AAC  
TAG CCA ATG AAT CTA AAT CTT CCC CTA AAG CTA CAA CGA CAA AAC GGT AAA AGG TTG  
▶ Ile Gly Tyr Leu Asp Leu Glu Gly Asp Phe Asp Val Ala Val Leu Pro Phe Ser Asn  
  
AGC ACA AAT AAC GGG TTA TTG TTT ATA AAT ACT ACT ATT GCC AGC ATT GCT GCT AAA  
TGG TGT TTA TTG CCC AAT AAC AAA TAT TTA TGA TAA CGG TCG TAA CGA CGA TTT  
▶ Ser Thr Asn Asn Gly Leu Leu Phe Ile Asn Thr Thr Ile Ala Ser Ile Ala Ala Lys

## KPI(-4-57; M15A, S17F)

XbaI  
GAA GAA GGG GTA TCT CTA GAT AAA AGA GAG GTT GTT AGA GAG GTG TGC TCT GAA CAA  
CTT CTT CCC CAT AGA GAT CTA TTT TCT CTC CAA CAA TCT CTC CAC ACG AGA CTT GTT  
▶ Glu Glu Gly Val Ser Leu Asp Lys Arg Glu Val Val Arg Glu Val Cys Ser Glu Gln

## RsrII

## AgeI

## AatII

GCT GAG ACC GGT CCG TGC CGT GCA GCT ATC TTC CGC TGG TAC TTT GAC GTC ACT GAA  
CGA CTC TGG CCA GGC ACG GCA CGT CGA TAG AAG GCG ACC ATG AAA CTG CAG TGA CTT  
▶ Ala Glu Thr Gly Pro Cys Arg Ala Ala Ile Phe Arg Trp Tyr Phe Asp Val Thr Glu  
  
GGT AAG TGC GCT CCA TTC TTT TAC GGC GGT TGC GGC GGC AAC CGT AAC AAC TTT GAC  
CCA TTC ACG CGA GGT AAG AAA ATG CCG CCA ACG CCG CCG TTG GCA TTG TTG AAA CTG  
▶ Gly Lys Cys Ala Pro Phe Phe Tyr Gly Gly Cys Gly Gly Asn Arg Asn Asn Phe Asp

## BamHI

## HindIII

ACT GAA GAG TAC TGC ATG GCA GTG TGC GGA TCC GCT ATT TAA GCT T  
TGA CTT CTC ATG ACG TAC CGT CAC ACG CCT AGG CGA TAA ATT CGA A  
▶ Thr Glu Glu Tyr Cys Met Ala Val Cys Gly Ser Ala Ile

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Figure 45

Plasma kallikrein inhibition by KPI (-4-57) variants

<u>Variant</u>		<u>Substitution</u>			<u>K<sub>i</sub>(nM)</u>
		15	16	17	
TW113	KPI (-4-57)				45.00
DD185	KPI (-4-57; M15A, S17F)	A		F	0.39
TW6165	KPI (-4-57; M15A, S17W)	A		W	0.65
TW6166	KPI (-4-57; M15A, S17Y)	A		Y	0.40
TW6175	KPI (-4-57; M15L, S17F)	L		F	0.50
BG028	KPI (-4-57; M15L, S17Y)	L		Y	1.10
TW6183	KPI (-4-57; I16H, S17F)		H	F	1.20
TW6184	KPI (-4-57; I16H, S17Y)		H	Y	0.91
TW6185	KPI (-4-57; I16H, S17W)		H	W	1.30
TW6173	KPI (-4-57; M15A, I16H)	A	H		1.00
TW6174	KPI (-4-57; M15L, I16H)	L	H		0.90

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FIGURE 46A

Variant	Sequence	Inhibition Ki (nM)		
		kallikrein	Plasmin	Xa
Aprotinin	RPDFCLEPPYTGPKARIIRFYFNKAGLCQTFVYGGCRKRNNFKSAEDCHRTCGGA	20.00	0.23	5000.0
Aprotinin R15, S42	DFCLEPPYTGPKARIIRFYFNKAGLCQTFVYGGCRKRNNFKSAEDCHRTCGGA	0.91	0.17	3983.0
KPI (-4-57)	EVRVCSQAETGPKRAMISRWFYDVTEGKCAPFFYGGCGNRNNFDTEEYCHAVCGSAI	45.00	34.00	3718.0
TW6167	EVRVCSQAETGPKRAMISRWFYDVTEGKCAPFFYGGCGNRNNFDTEEYCHAVCGSAI	61.00		3641.0
BG031	EVRVCSQAETGPKRAMISRWFYDVTEGKCAPFFYGGCGNRNNFDTEEYCHAVCGSAI	34.00		498.0
BG032	EVRVCSQAETGPKRAMISRWFYDVTEGKCAPFFYGGCGNRNNFDTEEYCHAVCGSAI	49.00		731.0
TW101	EVCSEAETGPKRAMISRWFYDVTEGKCAPFFYGGCGNRNNFDTEEYCHAVCGSAI	2000.00	11.50	
TW6208	EVRVCSQAETGPKRAMISRWFYDVTEGKCAPFFYGGCGNRNNFDTEEYCHAVCGSAI			369.0
TW106	EVCSEAETGPKRAMISRWFYDVTEGKCAPFFYGGCGNRNNFDTEEYCHAVCGSAI	560.00	3.70	
DD108	EVRVCSQAETGPKRAMISRWFYDVTEGKCAPFFYGGCGNRNNFDTEEYCHAVCGSAI	1.70	11.20	1600.0
DD109	EVRVCSQAETGPKRAMISRWFYDVTEGKCAPFFYGGCGNRNNFDTEEYCHAVCGSAI	9.50		1681.0
DD110	EVRVCSQAETGPKRAMISRWFYDVTEGKCAPFFYGGCGNRNNFDTEEYCHAVCGSAI	2.10		624.0
DD111	EVRVCSQAETGPKRAMISRWFYDVTEGKCAPFFYGGCGNRNNFDTEEYCHAVCGSAI	5.60		
DD112	EVRVCSQAETGPKRAMISRWFYDVTEGKCAPFFYGGCGNRNNFDTEEYCHAVCGSAI	6.80		998.0
TW6179	EVRVCSQAETGPKRAMISRWFYDVTEGKCAPFFYGGCGNRNNFDTEEYCHAVCGSAI	78.00		368.0
TW6163	EVRVCSQAETGPKRAMISRWFYDVTEGKCAPFFYGGCGNRNNFDTEEYCHAVCGSAI	4.70	103.58	4532.0
TW6172	EVRVCSQAETGPKRAMISRWFYDVTEGKCAPFFYGGCGNRNNFDTEEYCHAVCGSAI	315.00		1463.0
TW6180	EVRVCSQAETGPKRAMISRWFYDVTEGKCAPFFYGGCGNRNNFDTEEYCHAVCGSAI	70.00		885.0
TW6181	EVRVCSQAETGPKRAMISRWFYDVTEGKCAPFFYGGCGNRNNFDTEEYCHAVCGSAI	150.00		1514.0
BG001	EVRVCSQAETGPKRAMISRWFYDVTEGKCAPFFYGGCGNRNNFDTEEYCHAVCGSAI	38.00	10.00	489.0
TW116	EVCSEAETGPKRAMISRWFYDVTEGKCAPFFYGGCGNRNNFDTEEYCHAVCGSAI	145.00	89.00	806.0
DD102	EVRVCSQAETGPKRAMISRWFYDVTEGKCAPFFYGGCGNRNNFDTEEYCHAVCGSAI	16.00		315.0
DD103	EVRVCSQAETGPKRAMISRWFYDVTEGKCAPFFYGGCGNRNNFDTEEYCHAVCGSAI	17.00		2128.0
DD104	EVRVCSQAETGPKRAMISRWFYDVTEGKCAPFFYGGCGNRNNFDTEEYCHAVCGSAI	15.00		237.0
DD105	EVRVCSQAETGPKRAMISRWFYDVTEGKCAPFFYGGCGNRNNFDTEEYCHAVCGSAI	18.00		198.0
TW6168	EVRVCSQAETGPKRAMISRWFYDVTEGKCAPFFYGGCGNRNNFDTEEYCHAVCGSAI	25.80		3521.0
TW6182	EVRVCSQAETGPKRAMISRWFYDVTEGKCAPFFYGGCGNRNNFDTEEYCHAVCGSAI	36.00		752.0
TW6194	EVRVCSQAETGPKRAMISRWFYDVTEGKCAPFFYGGCGNRNNFDTEEYCHAVCGSAI	70.83		
TW6210	EVRVCSQAETGPKRAMISRWFYDVTEGKCAPFFYGGCGNRNNFDTEEYCHAVCGSAI	54.00		277.0
CL006	EVRVCSQAETGPKRAMISRWFYDVTEGKCAPFFYGGCGNRNNFDTEEYCHAVCGSAI	110.20		89600.0
BG012	EVRVCSQAETGPKRAMISRWFYDVTEGKCAPFFYGGCGNRNNFDTEEYCHAVCGSAI			40.0
				116.0

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FIGURE 46B

TW6209	EVVREVCSEQAETGPCRAMISRWYFDVTEGKCAPFFYGGCGGNRRNFDTEEYCNVAVCGSAI	81.00	45.90	184.0	613.0
TW6211	EVVREVCSEQAETGPCRAMISRWYFDVTEGKCAPFFYGGCGGNRRNFDTEEYCNVAVCGSAI	184.00		402.0	
DD128	EVVREVCSEQAETGPCRAMISRWYFDVTEGKCAPFFYGGCGGNRRNFDTEEYCNVAVCGSAI	44.00			37.0
TW6142	EVVREVCSEQAETGPCRAMISRWYFDVTEGKCAPFFYGGCGGNRRNFDTEEYCNVAVCGSAI	18.00	18.00	7972.0	225.0
AL301	EVVREVCSEQAETGPCRAMISRWYFDVTEGKCAPFFYGGCGGNRRNFDTEEYCNVAVCGSAI	216.00		1557.0	
AL302	EVVREVCSEQAETGPCRAMISRWYFDVTEGKCAPFFYGGCGGNRRNFDTEEYCNVAVCGSAI	39.00			316.0
TW6147	EVVREVCSEQAETGPCRAMISRWYFDVTEGKCAPFFYGGCGGNRRNFDTEEYCNVAVCGSAI	35.00		1090.0	179.0
TW6138	EVVREVCSEQAETGPCRAMISRWYFDVTEGKCAPFFYGGCGGNRRNFDTEEYCNVAVCGSAI	18.00		921.0	309.0
TW6154	EVVREVCSEQAETGPCRAMISRWYFDVTEGKCAPFFYGGCGGNRRNFDTEEYCNVAVCGSAI	11.00		915.0	39.0
TW6155	EVVREVCSEQAETGPCRAMISRWYFDVTEGKCAPFFYGGCGGNRRNFDTEEYCNVAVCGSAI	11.00			27.0
TW6140	EVVREVCSEQAETGPCRAMISRWYFDVTEGKCAPFFYGGCGGNRRNFDTEEYCNVAVCGSAI	35.00		475.0	
TW6156	EVVREVCSEQAETGPCRAMISRWYFDVTEGKCAPFFYGGCGGNRRNFDTEEYCNVAVCGSAI				
TW6141	EVVREVCSEQAETGPCRAMISRWYFDVTEGKCAPFFYGGCGGNRRNFDTEEYCNVAVCGSAI	42.00			
TW118	EVCSEQAETGPCRAMISRWYFDVTEGKCAPFFYGGCGGNRRNFDTEEYCNVAVCGSAI	6.00	24.00	13009.0	68.0
DD100	EVVREVCSEQAETGPCRAMISRWYFDVTEGKCAPFFYGGCGGNRRNFDTEEYCNVAVCGSAI	15.00			
TW6157	EVVREVCSEQAETGPCRAMISRWYFDVTEGKCAPFFYGGCGGNRRNFDTEEYCNVAVCGSAI	40.00		511.0	168.0
TW6158	EVVREVCSEQAETGPCRAMISRWYFDVTEGKCAPFFYGGCGGNRRNFDTEEYCNVAVCGSAI	29.00			
TW6159	EVVREVCSEQAETGPCRAMISRWYFDVTEGKCAPFFYGGCGGNRRNFDTEEYCNVAVCGSAI	17.00			64.0
TW6161	EVVREVCSEQAETGPCRAMISRWYFDVTEGKCAPFFYGGCGGNRRNFDTEEYCNVAVCGSAI	7.50	18.00	1507.0	8.7
DD101	EVVREVCSEQAETGPCRAMISRWYFDVTEGKCAPFFYGGCGGNRRNFDTEEYCNVAVCGSAI	64.00		924.0	
TW6151	EVVREVCSEQAETGPCRAMISRWYFDVTEGKCAPFFYGGCGGNRRNFDTEEYCNVAVCGSAI	163.00		1162.0	954.0
TW6139	EVVREVCSEQAETGPCRAMISRWYFDVTEGKCAPFFYGGCGGNRRNFDTEEYCNVAVCGSAI	19.00	22.80	152.0	78.0
TW6153	EVVREVCSEQAETGPCRAMISRWYFDVTEGKCAPFFYGGCGGNRRNFDTEEYCNVAVCGSAI	11.20	21.30	65.0	36.0
TW122	EVCSEQAETGPCRAMISRWYFDVTEGKCAPFFYGGCGGNRRNFDTEEYCNVAVCGSAI	32.00	27.00		581.0
TW6178	EVVREVCSEQAETGPCRAMISRWYFDVTEGKCAPFFYGGCGGNRRNFDTEEYCNVAVCGSAI	16.00		444.0	
TW6148	EVVREVCSEQAETGPCRAMISRWYFDVTEGKCAPFFYGGCGGNRRNFDTEEYCNVAVCGSAI	40.00			
TW124	EVCSEQAETGPCRAMISRWYFDVTEGKCAPFFYGGCGGNRRNFDTEEYCNVAVCGSAI	64.00	48.00		
TW6149	EVVREVCSEQAETGPCRAMISRWYFDVTEGKCAPFFYGGCGGNRRNFDTEEYCNVAVCGSAI	54.00			
TW6173	EVVREVCSEQAETGPCRAMISRWYFDVTEGKCAPFFYGGCGGNRRNFDTEEYCNVAVCGSAI	1.00	7.24	1432.0	
TW6174	EVVREVCSEQAETGPCRAMISRWYFDVTEGKCAPFFYGGCGGNRRNFDTEEYCNVAVCGSAI	0.90	6.89	2796.0	
BG002	EVVREVCSEQAETGPCRAMISRWYFDVTEGKCAPFFYGGCGGNRRNFDTEEYCNVAVCGSAI	0.98	19.00	403.0	60.0
DD129	EVVREVCSEQAETGPCRAMISRWYFDVTEGKCAPFFYGGCGGNRRNFDTEEYCNVAVCGSAI	3.60		1864.0	6.0
DD185	EVVREVCSEQAETGPCRAMISRWYFDVTEGKCAPFFYGGCGGNRRNFDTEEYCNVAVCGSAI	0.39	8.71	150.0	196.0

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FIGURE 46C

TW6165	EVVREVCSEQAETGPCRAAIIRWYFDVTEGKCAPFFYGGCGGNRRNFFDTEEYCHAVCGSAI	0.65	16.40	206.0	
TW6166	EVVREVCSEQAETGPCRAAIIRWYFDVTEGKCAPFFYGGCGGNRRNFFDTEEYCHAVCGSAI	0.4	10.10	73.0	
BG028	EVVREVCSEQAETGPCRALIIRWYFDVTEGKCAPFFYGGCGGNRRNFFDTEEYCHAVCGSAI	1.10	12.10	93.8	
TW6169	EVVREVCSEQAETGPCRALIIRWYFDVTEGKCAPFFYGGCGGNRRNFFDTEEYCHAVCGSAI	1.20		619.0	111.0
DD113	EVVREVCSEQAETGPCRALIPRWYFDVTEGKCAPFFYGGCGGNRRNFFDTEEYCHAVCGSAI	0.85	12.80	293.0	74.0
TW6175	EVVREVCSEQAETGPCRALIFRWYFDVTEGKCAPFFYGGCGGNRRNFFDTEEYCHAVCGSAI	0.50	7.46	35.0	56.0
TW6201	EVVREVCSEQAETGPCRAGIIRWYFDVTEGKCAPFFYGGCGGNRRNFFDTEEYCHAVCGSAI	34.60		419.0	
TW6202	EVVREVCSEQAETGPCRAGIIRWYFDVTEGKCAPFFYGGCGGNRRNFFDTEEYCHAVCGSAI	128.50		1237.0	
TW6203	EVVREVCSEQAETGPCRAGIPRWYFDVTEGKCAPFFYGGCGGNRRNFFDTEEYCHAVCGSAI	31.20		5045.0	
TW6204	EVVREVCSEQAETGPCRAAIIRWYFDVTEGKCAPFFYGGCGGNRRNFFDTEEYCHAVCGSAI			147.0	87.0
TW6205	EVVREVCSEQAETGPCRAAIIRWYFDVTEGKCAPFFYGGCGGNRRNFFDTEEYCHAVCGSAI			195.0	29.0
DD114	EVVREVCSEQAETGPCRAAIIRWYFDVTEGKCAPFFYGGCGGNRRNFFDTEEYCHAVCGSAI	0.70	7.77	224.0	
TW6190	EVVREVCSEQAETGPCRAAIIRWYFDVTEGKCAPFFYGGCGGNRRNFFDTEEYCHAVCGSAI	0.83	52.20	589.0	1396.0
TW6183	EVVREVCSEQAETGPCRAAIIRWYFDVTEGKCAPFFYGGCGGNRRNFFDTEEYCHAVCGSAI	1.20	11.68	12440.0	159.0
TW6184	EVVREVCSEQAETGPCRAAIIRWYFDVTEGKCAPFFYGGCGGNRRNFFDTEEYCHAVCGSAI	0.91	11.96	14000.0	214.0
TW6185	EVVREVCSEQAETGPCRAAIIRWYFDVTEGKCAPFFYGGCGGNRRNFFDTEEYCHAVCGSAI	1.30	18.60	388.0	473.0
BG003	EVVREVCSEQAETGPCRAAIIRWYFDVTEGKCAPFFYGGCGGNRRNFFDTEEYCHAVCGSAI	36.00		467.0	
TW6186	EVVREVCSEQAETGPCRAAIIRWYFDVTEGKCAPFFYGGCGGNRRNFFDTEEYCHAVCGSAI	0.48	8.86	186.0	11.0
TW6187	EVVREVCSEQAETGPCRAAIIRWYFDVTEGKCAPFFYGGCGGNRRNFFDTEEYCHAVCGSAI	3.80	15.40	92.0	15.0
TW6188	EVVREVCSEQAETGPCRAAIIRWYFDVTEGKCAPFFYGGCGGNRRNFFDTEEYCHAVCGSAI	4.00		419.0	24.0
TW6189	EVVREVCSEQAETGPCRAAIIRWYFDVTEGKCAPFFYGGCGGNRRNFFDTEEYCHAVCGSAI	4.00			34.0
TW6170	EVVREVCSEQAETGPCRAAIIRWYFDVTEGKCAPFFYGGCGGNRRNFFDTEEYCHAVCGSAI	2.50			452.0
DD115	EVVREVCSEQAETGPCRAAIIRWYFDVTEGKCAPFFYGGCGGNRRNFFDTEEYCHAVCGSAI			213.0	299.0
DD170	EVVREVCSEQAETGPCRAAIIRWYFDVTEGKCAPFFYGGCGGNRRNFFDTEEYCHAVCGSAI	0.99	18.00	550.0	
TW6176	EVVREVCSEQAETGPCRAAIIRWYFDVTEGKCAPFFYGGCGGNRRNFFDTEEYCHAVCGSAI	3.50	118.00	56.0	
TW6177	EVVREVCSEQAETGPCRAAIIRWYFDVTEGKCAPFFYGGCGGNRRNFFDTEEYCHAVCGSAI	7.20	32.70	245.0	156.0
BG006	EVVREVCSEQAETGPCRAAIIRWYFDVTEGKCAPFFYGGCGGNRRNFFDTEEYCHAVCGSAI	0.30	12.10	80.0	
DD130	EVVREVCSEQAETGPCRAAIIRWYFDVTEGKCAPFFYGGCGGNRRNFFDTEEYCHAVCGSAI	5.50			9.5
DD131	EVVREVCSEQAETGPCRAAIIRWYFDVTEGKCAPFFYGGCGGNRRNFFDTEEYCHAVCGSAI	7.90	2.00	1385.0	3.3
DD132	EVVREVCSEQAETGPCRAAIIRWYFDVTEGKCAPFFYGGCGGNRRNFFDTEEYCHAVCGSAI	112.00			16.8
DD120	EVVREVCSEQAETGPCRAAIIRWYFDVTEGKCAPFFYGGCGGNRRNFFDTEEYCHAVCGSAI	8.30			11.0
DD121	EVVREVCSEQAETGPCRAAIIRWYFDVTEGKCAPFFYGGCGGNRRNFFDTEEYCHAVCGSAI	19.00			21.0
BG014	EVVREVCSEQAETGPCRAAIIRWYFDVTEGKCAPFFYGGCGGNRRNFFDTEEYCHAVCGSAI	9.20	18.70	18.0	



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FIGURE 46D

DD122	EVVREVCSEQAETGPPCRALIFAWYFDVTEGKCAPFFYGGCGGNRNNFDTTEYCHAVCGSAI	15.00			46.0
BG015	EVVREVCSEQAETGPPCRALIYHWYFDVTEGKCAPFFYGGCGGNRNNFDTTEYCHAVCGSAI	6.00	12.20	19.4	597.0
BG020	EVVREVCSEQAETGPPCRAAIHKWYFDVTEGKCAPFFYGGCGGNRNNFDTTEYCHAVCGSAI	1.70		106.0	
BG022	EVVREVCSEQAETGPPCRAAIYHWYFDVTEGKCAPFFYGGCGGNRNNFDTTEHCHAVCGSAI	0.64	7.26	14.5	
BG023	EVVREVCSEQAETGPPCRALIYHWYFDVTEGKCAPFFYGGCGGNRNNFDTTEYCHAVCGSAI	23.00		262.0	
BG024	EVVREVCSEQAETGPPCRALIYHWYFDVTEGKCAPFFYGGCGGNRNNFDTTEYCHAVCGSAI	4.10	7.47	38.7	
BG027	EVVREVCSEQAETGPPCRAAIQHWYFDVTEGKCAPFFYGGCGGNRNNFDTTEYCHAVCGSAI	5.80		144.0	
DD116	EVVREVCSEQAETGPPCRAAIYHWYFDVTEGKCAPFFYGGCGGNRNNFDTTEYCHAVCGSAI	0.14		583.0	84.0
TW6191	EVVREVCSEQAETGPPCRAAIYHWYFDVTEGKCAPFFYGGCGGNRNNFDTTEYCHAVCGSAI	0.26		664.0	20.0
DD117	EVVREVCSEQAETGPPCRALIYHWYFDVTEGKCAPFFYGGCGGNRNNFDTTEYCHAVCGSAI	0.11		1034.0	99.0
BG029	EVVREVCSEQAETGPPCRALIYHWYFDVTEGKCAPFFYGGCGGNRNNFDTTEYCHAVCGSAI	3.20		7.9	
BG030	EVVREVCSEQAETGPPCRALIYHWYFDVTEGKCAPFFYGGCGGNRNNFDTTEYCHAVCGSAI	4.60		26.1	
BG033	EVVREVCSEQAETGPPCRAAIYHWYFDVTEGKCAPFFYGGCGGNRNNFDTTEHCHAVCGSAI	0.75		5.6	
BG034	EVVREVCSEQAETGPPCRAAIYHWYFDVTEGKCAPFFYGGCGGNRNNFDTTEYCHAVCGSAI	0.47		18.5	
BG040	EVVREVCSEQAETGPPCRALIYHWYFDVTEGKCAPFFYGGCGGNRNNFDTTEYCHAVCGSAI	3.40		8.6	
BG016	EVVREVCSEQAETGPPCRGAIQHWYFDVTEGKCAPFFYGGCGGNRNNFDTTEYCHAVCGSAI	160.00		178.0	
BG017	EVVREVCSEQAETGPPCRGAIYHWYFDVTEGKCAPFFYGGCGGNRNNFDTTEYCHAVCGSAI	180.00		200.0	
BG021	EVVREVCSEQAETGPPCRGSIYHWYFDVTEGKCAPFFYGGCGGNRNNFDTTEYCHAVCGSAI	340.00		224.0	
BG025	EVVREVCSEQAETGPPCRGLIYHWYFDVTEGKCAPFFYGGCGGNRNNFDTTEYCHAVCGSAI	65.00		16.2	
BG026	EVVREVCSEQAETGPPCRGAIYHWYFDVTEGKCAPFFYGGCGGNRNNFDTTEYCHAVCGSAI	50.00		34.9	
DD118	EVVREVCSEQAETGPPCRALHNRWYFDVTEGKCAPFFYGGCGGNRNNFDTTEYCHAVCGSAI	0.53			
DD134	EVVREVCSEQAETGPPCRALFKRWYFDVTEGKCAPFFYGGCGGNRNNFDTTEYCHAVCGSAI	1.10	1.05	15640.0	0.6
DD135	EVVREVCSEQAETGPPCRALFKRWYFDVTEGKCAPFFYGGCGGNRNNFDTTEYCHAVCGSAI	1.30		7473.0	0.9
DD136	EVVREVCSEQAETGPPCRALFKRWYFDVTEGKCAPFFYGGCGGNRNNFDTTEYCHAVCGSAI	1.10			1.8

Figure 47

VOLUMES

NS	344.25
KPI	245.75

	KPI	NS
	298	366
	266	342
	354	294
	258	385
	168	288
	266	469
	172	338
	184	272
MEAN	245.75	344.25
STDEV	66.2414415	63.97488346
TTEST	0.009094999	

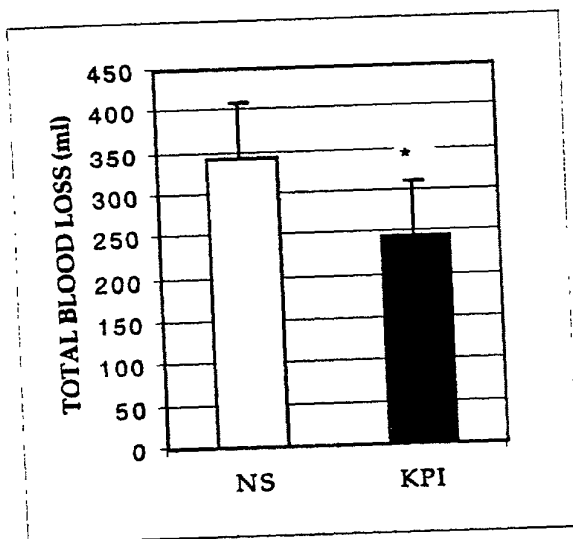


Figure 48

HEMOGLOBIN

NS	23.61
KPI	13.59

	KPI	NS
	16.58	24.95
	15.19	24.87
	20.21	20.46
	8.99	27.59
	14.63	18.23
	15.31	31.59
	7.7	23.26
	10.14	17.96
MEAN	13.59375	23.61375
STDEV	4.261438	4.68761
TTEST		0.000536

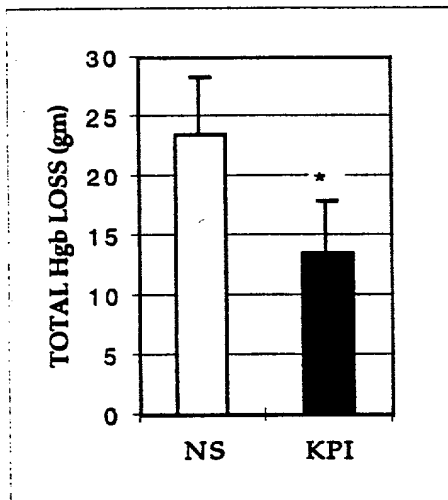


Figure 49

PaO<sub>2</sub>

	Baseline PaO <sub>2</sub>		End CPB		Obs 60 min		Obs 180 min	
	KPI	NS	KPI	NS	KPI	NS	KPI	NS
	652.2	670.9	495.7	60.5	483.7	441.3		391.3
	654	559.2	444.6	132.2	330.1	448.7	264.1	484.6
	596.2	622.9	170.2	93.8	415.4	85.1	416.5	81.3
	606.2	689.2	264.2	333.9	430.2	529.6	361.9	333.2
	633.1	665.1	567.2	341.7	613	568.3	90.8	546.6
	646.6	527	507.4	226.9	564.3	438.1	518.2	485.3
	563.2	461.7	547.1	89.1	501	42.6	494.2	45.6
	659.9	508	416.6	59.7	504.5	405.8	452	383.7
MEAN	626.425	588	426.625	167.225	480.275	369.938	371.1	344
STDEV	34.4692	85.5055	140.474	117.993	88.6187	196.523	150.277	186.22
	3	6	1	1	9	5	4	7
TTEST	p=	0.268	p=	0.0014	p=	0.17915	p=	0.76
	NS.				NS.			

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Figure 50

## Summary of Data

Total Volumes		Serial Chest tube Hbg				
Chest tube Sacrifice		0-30min	30-60min	60-120min	120-180min	
KPI-1	185	113	3.7	4.3	8.6	6.2
KPI-2	198	68	4.3	6.4	6.7	5.7
KPI-3	142	212	4.1	4.4	7	7.1
KPI-4	190	68	2.8	4	4.4	1.9
KPI-5	96	72	6.3	6.5	7	6.7
KPI-6	188	78	4.1	6.1	5.6	6.3
KPI-7	134	38	3.1	4.6	5.4	4.4
KPI-8	158	26	6.9	5.8	5.4	4.2
MEAN		4.41	5.26	6.26	5.3	
STDEV		1.45	1.04	1.32	1.72	

Total Hgb Loss		Serial Chest tube Hbg					
Total volume loss		0-30min	30-60min	60-120min	120-180min		
NS-1A	366	274	92	7.7	8.6	6.1	5.4
NS-2	342	236	106	7.2	7.4	7.6	7.1
NS-3	294	252	42	5.4	7.5	7.5	6.5
NS-4	385	303	82	8.4	7.2	7.1	6.3
NS-5	288	140	148	7.5	7.2	5.2	5.6
NS-6	469	261	208	4	7	7.3	7.4
NS-7	338	218	120	7.5	7.7	5.8	4.2
NS-8	272	206	66	7.4	8.2	6	5.3
MEAN	344.25	6.89	7.6	6.58	6.1		
STDEV	63.97	1.44	1.04	0.91	0.85		

Total Hgb Loss		Serial Chest tube Hbg					
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